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Award Number: DAMD17-95-1-5064

TITLE: Study of Chlamydia trachomatis in Military Women; Prevalence, Risk Factors, and a Cost Benefit Analysis of Early Diagnosis and Treatment

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REPORT DATE: September 1999

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	September 1999	Final (31 Aug 95 - 30 Aug 99)

4. TITLE AND SUBTITLE
Study of Chlamydia trachomatis in Military Women; Prevalence, Risk Factors, and a Cost Benefit Analysis of Early Diagnosis and Treatment

5. FUNDING NUMBERS
DAMD17-95-1-5064

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8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for public release; distribution unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 Words)*

In the 4th project year, 4,628 women were screened for chlamydia using urine LCR at Ft. Jackson, SC. 2,321 also submitted a self administered vaginal swab (SAS). Over the entire project period, at Ft. Jackson, there have been 23,010 female recruits at the Physical Exam Section (PES), 888 women at the Troop Medical Clinc (TMC), and 2,278 men have been screened for chlamydia. At Ft Bragg, 482 women were screened at a PAP clinic. **Methods:** After receiving instruction about chlamydia, subjects were asked for their informed consent to participate in the project. All enrolled subjects answered a chlamydia risk history questionnaire. Study participants submitted a first catch urine specimen and/or SAS for testing at Johns Hopkins by ligase chain reaction (LCR). Those that tested positive received azithromycin. **Results:** In the, 4th year, 629 women (10.0%) tested positive. Collection of urine over SAS was preferred by women and also performed better than SAS for detecting positives. In male recruits, the chlamydia prevalence was 5.2%. For the whole project, 2,189/23,010 (9.5%) female recruits were chlamydia positive. If young age ($\leq$ 25 years) were used as the sole screening criterion, 88.6% (20,388/23,010) of the recruit population would be tested, and 95.2 % of the positives would be identified. Young age was not a risk factor for men. **Conclusion:** We recommend screening women $\leq$ 25 years of age using urine-based screening in this population, as a clinically relevant cost-effective strategy to prevent development of PID and other sequelae.

14. SUBJECT TERMS
Women's Health

15. NUMBER OF PAGES
135

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)
Prescribed by ANSI Std. Z39-18
298-102

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Charlotte Gaydos 12-17-99

PI - Signature Date

4 Table of Contents

5 Introduction

Each year in the United States, there are approximately 4.5 million cases of *Chlamydia trachomatis* infection [1]. Although many *C. trachomatis* infections are asymptomatic [2] the symptoms and sequelae from infection, including cervicitis, urethritis, chronic pelvic pain, pelvic inflammatory disease (PID), ectopic pregnancy, and infertility represent a large disease burden [1,3]. Infection rates for young, sexually active women range from 5-20%. In men, chlamydia infections can cause urethritis, epididymitis, and proctitis [1,4,5]. *C. trachomatis* can be transmitted through vaginal, anal, and oral sex as well as mother-to-infant. Risk factors in women for infection include having cervical ectopy, being a young female, having multiple sex partners, and inconsistent condom use [1,6,7,8]. Detection of genital *C. trachomatis* infection by ligase chain reaction (LCR) using first void urine is a non-invasive, highly sensitive, and highly specific procedure [9,10]. Although the cost of LCR is higher than other tests, it is more sensitive and more specific [11,12]. Culture costs more and is less sensitive than either LCR or PCR [9,13-17]. Recently, use of self-administered vaginal swabs (SAS) has also been shown to be a senstive and specific method to obtain specimens for DNA amplification[18-20].

In the U.S., the annual costs of chlamydia infections and their sequelae are estimated at $5 billion. Screening urine by LCR for the detection of *C. trachomatis* and treatment of those persons testing positive with a single dose therapy of azithromycin can prevent a large burden of disease caused by *C. trachomatis* infection. This grant has been in progress for four years. Based upon findings of the study, recommendations are made for a cost-effective chlamydia control program designed to reduce morbidity due to *C. trachomatis* in military women.

The objectives of this study were:

1. Determine the prevalence of infection in several military populations at risk of *C. trachomatis* infection including: female military recruits, and women attending the Troop Medical Clinic (TMC) with urogenital symptoms or the Pap Smear Clinic;
2. Determine risk factors predictive of infection;
3. Conduct a cost-effectiveness analysis comparing universal screening versus selective screening utilizing risk factor criteria;
4. Recommend a chlamydial control program: selective screening and treatment, universal screening and treatment, or mass therapy for all female basic recruits;
5. Monitor PID and ectopic pregnancy rates, over the period of chlamydia screening.
6. In addition to the aforementioned study objectives, we added an objective to screen incoming male recruits (2,278) to estimate prevalence in men in order to determine the reinfection potential of women undergoing the screening program. Risk factors for infection in male recruits were also studied.
7. Additionally, we added a study objective to determine whether the use of SAS as a diagnostic specimen was feasible in this population of primarily asymptomatic women.

Based on meeting these objectives, we recommend that young age ($\leq$25 years) would be a valid and cost-effective risk factor upon which to screen female recruits joining the U.S. Army for chlamydia and that rescreening at yearly intervals should be considered.

6 Body
6.1 Methods

STUDY SUBJECTS

Fort Jackson:

1. RECRUITS (PHYSICAL EXAM SECTION)

Urine Study:

Every Sunday, female recruits undergoing in processing at the Reception Battalion, Physical Examination Section or PES) Ft. Jackson were directed to a classroom to be educated about the transmission, symptoms, and sequelae of chlamydia by a research nurse. After giving their informed consent, subjects were then asked to participate in the study by filling out a demographic and risk behavior questionnaire and submitting a urine specimen (N = 23,010). The questionnaire was a one page, two-sided scanning form (Scantron Corporation, Tustin, CA). All specimens, consent forms, and questionnaires were shipped to Johns Hopkins University Chlamydia Laboratory, under appropriate environmental conditions (4^0 C for urine specimens).Only female recruits were screened with the exception of 2 periods when only male (n=2,278) recruits from the PES were screened.

To determine comparability of the volunteer and non-volunteer recruits at the Reception Battalion, with regard to demographics and risk history, a sub-sample of those non-volunteering recruits were invited to anonymously fill out a questionnaire. This sub-sample was collected on the first Sunday of each month from female recruits and during all four weeks of male recruit screening.

SAS Study:

During the months of March, 1999 to August, 1999, women who enrolled in the urine study at Ft. Jackson, were also asked to volunteer to provide a self-administered vaginal swab (SAS) for the detection of chlamydia by LCR, as well as asked to complete a questionnaire regarding the ease of use and preference for collection of urine versus SAS.

2. SYMPTOMATIC TROOP MEDICAL CLINIC.

On week days, during the years 1996-97, active duty symptomatic women (N=800) attending the Troop Medical Clinic (TMC) were enrolled into the study to determine the prevalence of chlamydia in symptomatic Army women. Procedures and information collected were the same as that described above for the recruit population.

Fort Bragg

During 196-1997, asymptomatic active duty women (N= 480) attending PAP clinics at Ft Bragg were similarly enrolled into the study. In addition to submitting a urine, a chlamydia culture was also obtained from the endocervix of the enrolled women by the attending clinician, in order to compare urine LRC results to results obtained by culture. There were 434 matching urine and cervical specimens for comparison purposes.

LABORAOTRY METHODS: CHLAMYDIA URINE LCR TESTS AND CULTURE

Urines were processed and tested by ligase chain reaction (LCR) (Abbott Laboratories,

Abbott Park, IL) for chlamydial DNA, according to manufacture's directions. The LCR test is cleared by the FDA for use with female and male urine specimens. At fort Bragg, cultures for chlamydia were performed according to standard protocol in the Chlamydia Research Lab at Johns Hopkins University

DATA MANAGEMENT AND ANALYSIS

The scan forms were scanned into an Ascii text format and then appended to the main data base stored initially as a D-baseIII file. The data system was updated to Access97 (Microsoft Corporation, Seattle, WA) in 1998. The LCR results, demographics, and risk factor information were analyzed using chi-squared tests, Fisher's exact tests and logistic regression analysis (Stata 4.0, College Station, TX). Data for the multivariate models were recorded as dichotomous variables (presence of risk vs. no risk or unknown risk) according to the findings of the univariate analysis. Quarterly reports generated through out the 4 years of the study are appended. Data from questionnaires regarding the use of SAS specimens were entered into an Access97 file and data similarly analyzed as above.

6.2 Results

FEMALE RECRUITS URINE STUDY, FT JACKSON, 1998-9 (4th year)

The volunteer rate from August 31, 1998 to August 15, 1999.was 79.9%. From the 6,270 participating female recruits, 87.2% (5,467/6,270) were age 25 or younger, 47.2% (2,960/6,270) were Caucasian, 35.7% (2,237/6,270) were African American, and 17.1% (1,073/6,270) were other races. The prevalence for *C. trachomatis* by LCR for the population was 10.0% (629/6,270).

FEMALE RECRUITS URINE STUDY, FT JACKSON, 1996-97(published article[21])

A thorough analysis of this population from January 1996 to December 1997 was completed for 13,223 female subjects presenting at the Physical Examination Section (See Appendix 11.1.1 for the full article) [21]. The infection status of nineteen individuals could not be determined due to missing data items or insufficient urine. Of the remaining 13,204 female recruits, the median age was 21 years (range 17 to 39) and 87.9% (11,603/13,204) were age 25 or younger. Half of the women were Caucasian, 35.9% were African American, and 13.1% were other races. The prevalence for *C. trachomatis* by urine ligase chain reaction for the entire population was 9.2%.

By questionnaire, 93.1% reported having had vaginal sex, 26.7% had more than 1 sex partner in the previous 90 days, 31.4% had a new sex partner in the previous 90 days, and only 16.9% always used condoms. A prior history of chlamydia infection was reported in 9.1%, gonorrhea in 3.3%, syphilis in 0.6%, and trichomonas infection in 4.6%. Of those volunteers who denied vaginal sex, 1.4% (13/914) were chlamydia positive, and of those who reported always using condoms, 8.4% (177/2,115) were chlamydia positive.

Of the 823 non-volunteer recruits who filled out a questionnaire anonymously, 203 (24.7%) did not provide age data and were dropped from the analysis. The remaining individuals had a mean age of 21 (range 17 to 36), 51.3% were Caucasian and 31.9% were African American and with regard to these characteristics the non-volunteers were not significantly different from volunteers. However, of the non-volunteers, only 66.9% reported

having vaginal sex compared to 93.1% of the volunteers ($p < 0.001$). In the non-volunteers, four variables were significantly different from those of the volunteers, even when vaginal sex was controlled for: only 4.0% reported prior chlamydia infections ($p = 0.013$), 18.2% had a new sex partner ($p = 0.002$), 20.1% consistently used condoms ($p < 0.001$), and 90.7% reported no previous STD diagnosis ($p = 0.001$). Of the non-volunteers, 17.7% had more than one sex partner in the prior 90 days, similar to the volunteers when controlling for vaginal sex ($p = 0.189$).

The age-specific prevalence of *C. trachomatis* infection for the 13,204 volunteers is shown in the published article (Fig. 1) [21]. The highest prevalence of chlamydia was in females aged 17 (12.2%) years. Prevalences declined sharply with increasing age to below 5% for ages older than 25 years. For further analysis, the youngest age categories (17 to 25 yr.) were combined into a variable called "young" (prevalence 10.0%, 1162/11,603). In the "older" category (ages 26 to39 yr.) the prevalence was 3.6% (57/1,601). By race, prevalences were 5.5% (369/6,715) for Caucasian, 14.9% (707/4,733) for African-American, and 8.1% (143/1,756) for other races.

UNIARIATE ANALYSIS

Univariate analysis identified 10 significant variables associated with chlamydia infection: young age (17 to 25 years), African-American race, ethnicity other than Caucasian or African American, ever having vaginal sex, > 1 sex partner in the previous 90 days, new sex partner in the previous 90 days, having inconsistently used condoms last 90 days, a previous diagnosis of gonorrhea, a previous diagnosis of trichomonas, and history of any sexually transmitted disease (published article, Table 2) [21]. Prior diagnosis of chlamydia or syphilis were not significantly associated with being chlamydia positive.

MULTIAVARIATE ANALYSIS

In the complete multivariate model, vaginal sex (odds ratio [O.R.] 5.9, 95% confidence interval [C.I.] 3.2, 10.6), young age (odds ratio 3.0, 95% confidence interval 2.3, 4.0), African American race (O.R. 3.4, 95% C.I. 2.9, 3.8), more than 1 sex partner (O.R. 1.4, 95% C.I. 1.2, 1.7), having a new sex partner (O.R. 1.3, 95% C.I. 1.1, 1.6), having inconsistently used condoms (O.R. 1.4, 95% C.I. 1.1, 1.6), and history of any sexually transmitted diseases (O.R. 1.2, 95% C.I. 1.0, 1.4) were independent predictors for chlamydia infection (published article, Table 3) [21].

STRATEGIES FOR SELECTIVE SCREENING CRITERIA FOR IDENTIFICATION OF CHLAMYDIA INFECTIONS.

A screening strategy using all variables identified as independent predictors would require testing 100% of the population, and would detect 100% of the positive individuals. In this model, the magnitude of risk associated with having a new sex partner may vary across race categories. For the purpose of a screening program, this would not alter the proportion of the population tested or the percent of positives detected using this model. Because screening based on race would likely be viewed as inequitable, a strategy excluding race was examined. This strategy would necessitate a questionnaire, and include those reporting high risk behaviors, such as more than one or a new sex partner in the previous 90 days, lack of condom use, prior sexually transmitted disease, or young age. Screening on these criteria would still require testing almost 100% of the population. If a questionnaire could be avoided and young age ($\leq$ 25 years)

used alone as the screening criterion, 87.9% (11,603/13,204) of the population would need to be tested, and 95.3 % (1,162/1,219) of the positives would be identified. We therefore recommend screening only women ≤ 25 years of age as a clinically relevant strategy.

FEMALE RECRUITS COMPLETE STUDY PERIOD URINE STUDY, FT. JACKSON (1996-99)

Overall at Ft. Jackson 23,010 female recruits were screened (either with urine alone, both urine and SAS, or SAS alone) with a volunteer rate of 80.3% and a prevalence of 9.5% (2,189/23,010). The prevalence by urine only was 9.4% (2,142/22,698). The prevalence for the small number who were also screened by SAS was 8.8% (204/2,321). Briefly, for this whole population of female recruits, the mean age was 20.6 years, 50.5% were Caucasian (5.4% positive), 35.6% African American (16.0% positive), 13.9% other Races (7.9% positive). Risk factor analysis: having vaginal sex, 90.9%; more than 1 sex partner in last 90 days, 26.0%; new sex partner in last 90 days, 29.6%; consistent condom use last 90 days, 16.1%. Variations in geographic distribution of "home of record" were observed. Figure 1 demonstrates the geographic variability by state for the "home of record" from which the female recruits entered military service. Prevalence for all years was 9.5%; for year 1996 8.51%; for year 1997 9.68%; for year 1998 9.90%; for year 1999 9.92%. Analyses of risk factor change for these years are being presented in abstract form for Prevention2000 and Sexually Transmitted Diseases for the Millennium (see appendices).

For description of complete study population, see appended Quarterly Report dated 11/8/99 attached in appendix for period 1/21/96 through 9/30/99. For statistical analysis of risk factors, see published paper (described above)[21].

TROOP MEDICAL CLINIC PREVALENCE STUDY IN SYMPTOMATIC WOMEN, FORT JACKSON, (1996-7)

Symptomatic women (N = 800) attending the TMC, were enrolled in our study, (approximate 80% volunteer rate). There were 92 (11.5%), who tested positive for chlamydia by urine LCR. A comparison was made for 519 women who had matching urine LCR results and results for cervical swabs specimens tested by the standard clinic method (Vidas, a commercial enzyme immunoassay). The chlamydia prevalence by urine LCR was 10.0% (52/519), while that by Vidas was 7.3% (38/519), a 26.9% increase in positives identified by LCR. Sensitivity for Vidas compared to LRC was 73.1% (38/52). Of the 672 which were statistically analyzed, 85% were age 25 or younger, 51.2% were African American, 12.5% had a prior history of chlamydia 96% reported vaginal sex, 23.7% had a new sex partner in the previous 90 days, 23.1% had more than one sex partner in the previous 90 days and 71% did not consistently use condoms. In those ≤ 25 years of age the chlamydia prevalence was 12.8%; 7.9% for caucasian and 15.4% for African American. The prevalence of chlamydia by risk category included: prior chlamydia 13.1%; vaginal sex, 12.3%; new sex partner, 12%; more than one sex partner, 13.6%; and inconsistent condom use, 11.6%.

PAP CLINICS PREVALENCE STUDY IN ASYMPTOMATIC WOMEN, FORT BRAGG STUDY (1996-97)

The study performed at Ft. Bragg was done to compare the sensitivity for urine LCR to the gold standard of culture with adjudication in 480 asymptomatic women attending a PAP clinic[22]. 465 women provided a urine specimen, and there were matching urine and cervical

specimens for 434. The prevalence by urine LCR was 7.3% compared to 5% by culture. Of the 11 additional positive urine LCR samples that were culture negative, all but one could be confirmed as true positives. There were 4 culture positive specimens, which were LCR negative. Thus, the sensitivity, specificity, positive and negative predictive values for urine LCR were 88.6%. 99.7%, 96.9%, and 99.0%, respectively. This study has been published in the Journal of Clinical Microbiology and is appended[22].

FEMALE RECRUITS SELF-ADMINISTERED SWAB STUDY , FT. JACKSON (1999)

The prevalence for the number who were screened by SAS was 8.8% (204/2,321). When results from SAS were compared to results obtained from urine testing for 2,009 matching specimens, there were 209 (10.4%) positive urine specimens, 180 (8.9%) positive by SAS , 157 (7.8%) positive for both urine and SAS, and 1,777 negative by both specimens. There were 52 specimens positive by urine and negative by SAS, while 23 were urine negative and SAS positive. Using the urine test as the gold standard, the sensitivity of SAS was 75.1% (157/209) and the specificity was 98.7% (1,777/1,800). See appended poster presentation for ICAAC, 1999. Preference data from this study indicated that approximately 60% of women submitting both urine and SAS stated they preferred to submit urine. However, when asked to submit either a urine or SAS, 93% submitted urine. This information has been submitted in abstract form to "Sexually Transmitted Infections for the Millennium" Meeting to be held in Baltimore in May, 2000 and is appended.

MALE RECRUITS URINE STUDY, FT JACKSON (1998)

There were 2,278 men screened, (volunteer rate 76.5%) the prevalence of infection was 5.3%. 2,245 had complete data and were further analyzed. The mean age was 20.6 (range 17-35) years, 59.5% were Caucasian, 27.3% were African American, and 13.2% were other races. 33.8% had more than one sex partner, and 36.7% had a new sex partner in the last 90 days. Only 21.2% of men reported using condoms regularly, and 2.6% reported having prior chlamydial infections. Of the men infected with *C. trachomatis*, only 14.4% reported having symptoms. In multivariate analysis, risk factors that proved useful for predicting chlamydial positivity included: African-American race, O.R. 4.1 (95% C.I. 2.7-6.1); more than one sex partner, O.R. 1.6 (95% C.I. 0.94-2.8); a new sex partner O.R. 1.7 (95% C.I. 1.0-2.9); and reported symptoms O.R. 4.5 (95% C.I. 2.5-8.1). Young age was not a risk factor, as it was for women. This information was presented at two conferences in abstract form (See Appendices). A manuscript is in preparation

6.3 Results in relation to statement of work

The Statement of Work as stated in the grant proposal included:

#1. Determine the prevalence of chlamydia infection by performing ligase chain (LCR) on urine specimens in 3 populations 1) incoming female recruits at Ft. Jackson, 2) symptomatic women attending the Troop Medical Clinic (TMC) at Ft. Jackson, and 3) in asymptomatic women attending a PAP clinic for the annual gynecological visit at Ft. Bragg.

Overall, for all sites, 26,570 women were screened. Prevalence of chlamydia infection for incoming female recruits was 9.5% (2,189/23,010). Prevalence of infection for symptomatic women attending the TMC was 11.5% (92/800). Prevalence of infection in asymptomatic

women attending a PAP clinic was 7.3%.

#2. The sensitivity and specificity of urine LCR will be calculated.

The sensitivity and specificity of urine LCR was determined to be 88.6% and 99.7%, compared to culture plus adjudcation of discrepant results respectively. See above.

#3. We will enter the demographic and risk factor information from each study participant into a computer data base.

We have established a large data base in ACCESS7 from which we have analyzed data, including all females and males enrolled in the study. The main data base rests independently from the SAS preference data, however, the two are linked by a unique identifier..

#4. Screening of up to 15,000 women by urine LCR at Ft. Jackson will continue.

We have screened a total of 23,010 female recruits at Ft. Jackson.

#5. We will determine by regression analysis which risk factors are predictive of being infected with chlamydia in each population type.

We have determined that although there are several risk factors predictive for chlamydia infection in women (see above), the simplest and most cost effective characteristic upon which to base a screening program is young age ($\leq$25 years).

#6. We will determine by cost analysis, sensitivity of risk factors to predict who is infected, and by prevalence whether it is more efficient to universally screen and treat, to selectively screen and treat, or to mass treat all female recruits with azithromycin.

Based on the results from the cost analysis results computed in the second year, we modeled that the mass therapy of all incoming female recruits would be the most cost-saving chlamydia control program for incoming recruits if the follow-up time was 5 years. See abstract appended by Howell et al. Presented at ICMASK.

7.We will institute a control program for incoming recruits using one of the above modalities. If the mass therapy option is to be used, there will be a control group. Up to 15,000 women will be screened by urine LCR, depending on which control program is instituted.

The universal screening and treatment of female military recruits was continued. Although we wished to test the mass therapy (universal treatment) program as a control program in the last year of the study in order to test the cost-effectiveness model which indicated mass therapy would be the most cost-saving control intervention, the Fort Jackson IRB (Eisenhower, Ft. Gordon) denied approval to test such an intervention. For this reason, universal screening of all female recruits and treatment of positives was continued as a control intervention program. Permission to have a mass treatment arm of the study was granted, however, by the Institutional Review Board (IRB) at Johns Hopkins. The Fort Jackson IRB response is attached in Appendix 11.4.

8.We will monitor incidence rates of pelvic inflammatory disease (PID) ectopic pregnancy rates, chronic pelvic pain, and acute respiratory disease rates for the women enrolled in each treatment arm of the study

We monitored rates for hospitalized pelvic inflammatory disease and ectopic pregnancy. Because we did not test the mass therapy option and did not expect the acute respiratory disease rates to be significantly affected by our program, we did not monitor the respiratory disease rates. Additionally, since outpatient data records at Ft. Jackson are not computerized, we could not monitor outpatient sequelae. The study entitled "Decreasing hospitalization rates in female U.S. Army recruits associated with a screening program for *Chlamydia trachomatis*" was presented at the Thirteenth Meeting of the International Society for Sexually Transmitted Diseases in Denver, July, 1999 and is appended. A manuscript is in preparation. Briefly, 28,074 females entering the Army from January 1, 1996 through December 31, 1997 were screened and treated for chlamydia and compared to 21,021 women who were not offered screening. Hospitalization rates were calculated per person-year. Relative risks were adjusted for age, race, education, and aptitude score. Adjusted relative risks (RR) using Poisson regression were determined. The RR of hospitalization for PID was 0.91 (95% C.I. 0.66-1.25) in those screened. The RR of hospitalization for any reason of the screened group was 0.92 (95% C.I. 0.87-0.96). Although the hospitalization rate for PID was not statistically significant, the rate for hospitalization for any reason was significant. Limitations of this study include the inability to measure outpatient treatment for PID.

9. We will use a conditional probability model to estimate the most efficient way to control chlamydial infections and reduce morbidity among women in the military.

We have performed a cost-effectiveness analysis using a decision model based on data from this study. The results of this analysis were published as an article entitled "Control of *Chlamydia trachomatis* infections in female Army recruits: Cost-effective screening and treatment in training cohorts to prevent pelvic inflammatory disease" in Sexually Transmitted Diseases by Howell et al. in October 1999,;26,519-526 and is appended. Briefly, using a conservative estimate of a hypothetical cohort of 10,000 women [approximately 20,000 females enter basic training per year in the Army] who intended to complete 2 years of military service, we determined outcomes for a 1 and 2 year follow-up. We demonstrated that at a 9.2% prevalence, no screening resulted in $220,900 in training and sequelae costs and 276 cases of PID. Screening by young age ($\leq$25 years) produced the lowest cost $217,600, over a 1 year period and prevented 222 cases of PID for a cost savings of $15 per case of PID prevented. Universal testing prevented an additional 11 cases of PID at a cost of $226,400 or costing $800 per additional case of PID prevented over age-based screening. Universal treatment would prevent an additional 32 cases of PID and cost $221,100, saving $167 per additional case of PID prevented over universal screening. Over a 2 year period, universal treatment provided the highest cost-savings and prevented the most disease. Thus, screening by age would provide a cost-savings to the Army over a 1 year period, while over a 2 year period, universal treatment would be the most cost-effective.

7 Key Research Accomplishments

- Screened 23,010 female recruits at Fort Jackson, SC by urine ligase chain reaction for *Chlamydia trachomatis*. Identified a chlamydia prevalence of 9.5% in this population by this technique.
- Screened 2,321 female recruits at Fort Jackson, SC by self administered vaginal swab (SAS) for *Chlamydia trachomatis*. Identified a chlamydia prevalence of 8.8% in this population by this technique.
- Screened 800 symptomatic female soldiers at Troop Medical Clinic (TMC) at Fort Jackson, SC by urine ligase chain reaction for *Chlamydia trachomatis*. Identified a chlamydia prevalence of 11.5% in this population by this technique.
- Screened 465 asymptomatic female soldiers attending PAP clinics at Fort Bragg, NC by urine ligase chain reaction for *Chlamydia trachomatis*. Identified a chlamydia prevalence of 7.3% in this population by this technique.
- Screened 2,278 male recruits at Fort Jackson, SC by urine ligase chain reaction for *Chlamydia trachomatis*. Identified a chlamydia prevalence of 5.3% in this population by this technique.
- Performed univariate and multivariate analyses of above populations for risk factors associated with chlamydia positivity.
- Evaluated sensitivity and specificity of urine ligase chain reaction compared to culture at Fort Bragg, NC.
- Evaluated sensitivity and specificity of self administered vaginal swab ligase chain reaction compared to urine ligase chain reaction at Fort Jackson, SC.
- Evaluated female preference for SAS compared to urine collection methodologies at Fort Jackson, SC.
- Developed a pooling algorithm for chlamydia screening urine by ligase chain reaction as a cost-saving measure.

8 Reportable Outcomes

Databases:
We have established a large database in ACCESS97 of over 26,000 records, as well as an independent database for SAS preference data. These two databases can be linked by a unique identifier. See appendices for scantron and questionnaire instruments.

Published five manuscripts:

1. Gaydos CA, Howell MR, Pare B, Clark KL, Ellis DA, Hendrix RM, et al. *Chlamydia trachomatis* infections in female military recruits. New Engl J Med 1998;339:739-744.

2. Gaydos CA, Howell MR, Quinn TC, Gaydos JC, et al. Use of ligase chain reaction of urine compared to cervical culture for the detection of *Chlamydia trachomatis* in an asymptomatic military population of pregnant and non-pregnant females attending PAP smear clinics. J. Clin. Micro. 1998;36:1300-1304.

3. Kacena, K.A., S.B. Quinn, M.R. Howell, T.C. Quinn, G.E. Madico, **C.A. Gaydos**. Pooling urine samples for the screening of genital *Chlamydia trachomatis* infection in asymptomatic women using ligase chain reaction (LCR). J. Clin Microbiol. 36:481-485, 1998.

4. Howell MR, Gaydos JC, McKee KT, Hendrix RM, Quinn TC, Gaydos CA. Control of *Chlamydia trachomatis* in Group Cohorts: Opportunity for Cost-Effective Prevention of Pelvic Inflammatory Disease in Female Military Recruits. Sexually Transmitted Diseases. 1999; 26:519-526.

5. Howell MR, McKee K, Quinn TC, Gaydos JC, Gaydos CA. Point of entry screening for *C. trachomatis* in young female recruits: who derives the benefit. (submitted)

Presented 22 abstracts and lectures:

1. Gaydos, C.A., G. Jaschek, M.R. Howell, B. Pare, K. Clark, D. Ellis, K, McKee, R. Hendrix, J. Gaydos, T.C. Quinn. *Chlamydia trachomatis* Infections in Female Military Recruits Diagnosed By Urine-LCR: Prevalence and Risk Factors. Proceed. Europ. Soc. Chlamydia Research. p 412, 1996.

2. Gaydos, C.A., ClarkK, Jaschek M, Howell MR, Pare B, Ellis D, McKee K, Hendrix R, Quinn TC, Gaydos J. *Chlamydia trachomatis* infections in female soldiers at Fort Jackson and Fort Bragg diagnosed by urine-LCR. U.S. Army Preventive Medicine Conference, Charlotte, NC. September 16-20, 1996.

3. Gaydos, C.A., D. Pham, M.R. Howell, B. Pare, D. Ellis, K. Clark, K. McKee, R. Hendrix, J. Gaydos, T.C. Quinn. Use of ligase chain reaction (LCR) to diagnose *C. trachomatis* in female soldiers at Ft. Bragg and Ft. Jackson. Ann. Meet. Amer. Soc. Microbiol. C-377, p 186, 1997.

4. Gaydos, C.A., Chlamydia screening in recruits (talk),Third Annual Uniformed Services Recruit and Trainee Health Care Symposium, Walter Reed Army Institute of Research, Washington, D.C. May 20. 1997.

5. Howell, M.R., K. McKee, D. Ellis, J. Gaydos, R. Hendrix, T.C. Quinn, C.A.Gaydos. Cost-effectiveness of screening vs. Mass therapy for *C. trachomatis* in female army recruits. Internat. Congress Sex. Transm. Dis.. 12th Annual Meet. #P 513, p 147, 1997.

6. Kacena, K., M.R. Howell, T.C. Quinn, C.A. Gaydos. Pooling urine samples for the screening of *Chlamydia trachomatis* in women by ligase chain reaction (LCR): Accuracy and cost-effectiveness. Internat. Congress Sex. Transm. Dis.. 12th Annual Meet. #O 261, p 104, 1997

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Personnel trained on this project:

1. Dorothy Ellis, Health Research Nurse
2. Pamela Syffus, Health Educator
3. Eleanor Howard, Research Nurse
4. Katherine Cline, Research Nurse
5. Bobbie Lynn Jones, Research Nurse
6. Martha Alsup, Research Nurse
7. Sandra Leister, Laboratory Technician
8. Diana Perkins, Laboratory Technician
9. Dien Pham, Laboratory Technician
10. Graciela Jaschek, Laboratory Technician
11. Jennifer Tawes, Laboratory Technician
12. Melissa Theodore, Laboratory Technician
13. Rene Howell, Data Analyst/Cost-Effectiveness
14. Jane Cecil, Infectious Disease Fellow

Additional Funding:

As a result of this project, a further study to obtain information on the chlamydia prevalence in male recruits was initiated. Funding was received from Health Promotion and Preventive

Medicine Initiative (HPPI) sponsored by the U.S Army Center for Health Promotion and Preventive Medicine, Aberdeen Proving Ground, MD.

9 Discussion, Conclusions, and Recommendations

Among recruits, risk factor analysis by multivariate logistic regression identified five independent, statistically significant, predictors for being infected with chlamydia: young age, African American, vaginal intercourse, more than one new sex partner, and a new sex partner in the prior 90 days. Women that volunteered from the recruit population appeared to have behavioral characteristics that put them at high risk for chlamydial infections. Women, who were non-volunteers appeared to be similar demographically and many also practiced high risk behavior, but were significantly less likely to have these risk factors (prior chlamydia infection, vaginal sex, new sex partner, more than one sex partner, and inconsistent condom use) than were the volunteers.

Consistent with the findings of the risk factor analysis noted above and documented in the New England Journal of Medicine publication, young age (i.e., age 25 or less) was the only factor available for practical use (i.e., facilitated access to data and high political feasibility) which was significantly associated (O.R. 3.0) with chlamydial infection in the female recruits screened at Fort Jackson, SC. Additionally, this screening strategy provides a cost-savings over no screening.

Although the women from the symptomatic (TMC) and asymptomatic (PAP) groups had prevalences that were higher than the recruit population, their demographic and risk factor profiles were similar. The numbers of women enrolled were insufficient to perform univariate or multivariate regression analyses once characteristic stratifications were performed.

Discussions amongst the investigators have determined that in the absence of data on sex mixing patterns after basic training, reinfection, and lack of longitudinal screening programs, conduct of the cost-effectiveness analyses from primarily a one-year analytic horizon, was most relevant to the goals of this study due to potential for re-infection. Consequently, the cost-effectiveness analysis was conducted from a one-year and a two-year analytic horizon which considered only PID and chronic pelvic pain prevented. At the one year analytic horizon, screening based on young age was the most cost-effective and at the 2 year analytic horizon, universal treatment with azithromycin of a new female recruits was modeled to be the most cost-effective.

Screening efforts for male recruits identified a *C. trachomatis* prevalence of 5.3%. Chlamydial infections in over 2,200 men which directly impacts re-infection rates in female recruits, limiting the ability of only one screening event to prevent sequelae in females. Documentation of the extent of infection in male recruits provided preliminary data to determine this potential of re-infection in women. Our group has subsequently obtained funding for a more thorough study of chlamydia infections in male recruits, which uses an educational intervention with assessment of knowledge gained. Funding for this one year project was from the "Health Promotion and Preventive Medicine Initiative" sponsored by the U.S. Army Center for Health Promotion and Preventive Medicine, Aberdeen Proving Ground, MD.

In order to assess the impact of our chlamydia screening program on hospitalizations in the group offered screening during the first 3 years, we performed a prospective study. Hospitalizations (PASBA) for PID (ICD9 codes 614 and 615), infertility (ICD9 code 628), and

ectopic pregnancy (ICD9 code 633) in Army enlisted females with less than or equal to one year of service were examined per person year for 1996 and 1997. Denominator data were collected from the Defense Manpower Data Center, Monterey, CA. The Army recruits screened group were followed for hospitalization for all causes, PID, and ectopic pregnancy. Cases are comprised of only those subjects that entered full-time active duty and exclude those going from basic training at Fort Jackson into the reserves who would not be hospitalized in the military healthcare system unless on temporary active duty. The remaining females (not offered screening group) entering the Army as enlisted soldiers during the same time period in which the cases were gained (as per DMDC) comprised the remainder of the cohort. The cohort was followed for hospitalization up to 3 years of service. The relative risk for hospitalizations for any reason in the group of recruits offered chlamydia screening (with treatment of those infected) was significantly less than for recruits entering the Army who were not offered screening.

Another Women's Defense Grant (P.I. Anne Rompalo, M.D.) conducted at Fort Bragg, also a collaborative effort between Johns Hopkins and the Army, has found self-administered vaginal swabs (SAS) to be a potentially convenient alternative to the use of cervical and urine specimens with high sensitivity and specificity when used in **symptomatic** women in a clinic situation with one-on-one instruction. Others have also found the use of SAS to provide a sensitive and specific way to identify *C. trachomatis* in **symptomatic** women which is highly acceptable [19]. To assess the potential feasibility of future use of self-administered swabs in a non-clinic situation with a large group of **asymptomatic** women, we implemented a study for use of SAS with a questionnaire for the women in the urine screening study. They were asked to volunteer with informed consent to also join the SAS study. We determined the preferences of the female recruits with regard to screening test procedure. We asked them to provide a SAS in addition to the urine sample. Unfortunately, the SAS did not perform as well as the urine specimen in this study (sensitivity of 75.1% compared to urine) and the preference for collection of a screening sample was clearly for urine. When collecting both specimens, 60% of women preferred urine. When asked to collect either a SAS or a urine, 93% provided urine. Although the SAS has performed well in symptomatic women in other studies, we cannot recommend it as being satisfactory for screening in large groups in non-clinic venues as in this primarily young asymptomatic group of recruits.

In summary, urine-based screening for *C. trachomatis* by Ligase Chain Reaction was effective in a female military recruit population, as well as in a symptomatic Troop Medical Clinic population and an asymptomatic PAP clinic population. Acceptance was high, the urine specimens were readily obtained, and the assays were able to be performed quickly and efficiently. The study has demonstrated a high prevalence (9.5%) for female recruits from a geographically and demographically diverse group, a substantial prevalence (11.9%) from a symptomatic Troop Medical Clinic population, and a higher than expected prevalence (7.3%) from an asymptomatic PAP clinic population. We have demonstrated that screening and treating chlamydia infections in these women is cost-effective even from a one year analytic horizon. We have also shown that a chlamydia control program can reduce hospitalizations in female recruits. These results have indicated the need for an ongoing chlamydial control program in such female military groups.

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11 Appendices

BEST AVAILABLE COPY OF APPENDICES

11.1 Articles published or submitted during the project period: reference list and copies of abstracts

1. Gaydos CA, Howell MR, Pare B, Clark KL, Ellis DA, Hendrix RM, et al. *Chlamydia trachomatis* infections in female military recruits. New Engl J Med 1998;339:739-744.

2. Gaydos CA, Howell MR, Quinn TC, Gaydos JC, et al. Use of ligase chain reaction of urine compared to cervical culture for the detection of *Chlamydia trachomatis* in an asymptomatic military population of pregnant and non-pregnant females attending PAP smear clinics. J. Clin. Micro. 1998;36:1300-1304.

3. Kacena, K.A., S.B. Quinn, M.R. Howell, T.C. Quinn, G.E. Madico, **C.A. Gaydos**. Pooling urine samples for the screening of genital *Chlamydia trachomatis* infection in asymptomatic women using ligase chain reaction (LCR). J. Clin Microbiol. 36:481-485, 1998.

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5. Howell MR, McKee K, Quinn TC, Gaydos JC, Gaydos CA. Point of entry screening for *C. trachomatis* in young female recruits: who derives the benefit. (submitted)

CHLAMYDIA TRACHOMATIS INFECTIONS IN FEMALE MILITARY RECRUITS

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ABSTRACT

Background Asymptomatic genital *Chlamydia trachomatis* infections in women can lead to pelvic inflammatory disease, infertility, and ectopic pregnancy. To design a chlamydia-control program, we conducted a large survey of women in the U.S. military.

Methods From January 1996 through December 1997, urine samples from 13,204 new female U.S. Army recruits from 50 states were screened by ligase chain reaction for *C. trachomatis* infection. Information on potential risk factors was obtained by questionnaire. With multivariate analysis, we identified criteria for a screening program.

Results The overall prevalence of chlamydial infection was 9.2 percent, with a peak of 12.2 percent among the 17-year-old recruits. The prevalence was 15 percent or more among the recruits from five southern states. The following risk factors were independently associated with chlamydial infection: having ever had vaginal sex (odds ratio for infection, 5.9), being 25 years of age or less (odds ratio, 3.0), being black (odds ratio, 3.4), having had more than one sex partner in the previous 90 days (odds ratio, 1.4), having had a new partner in the previous 90 days (odds ratio, 1.3), having had a partner in the previous 90 days who did not always use condoms (odds ratio, 1.4), and having ever had a sexually transmitted disease (odds ratio, 1.2). A screening program for subjects 25 years of age or less (87.9 percent of our sample) would have identified 95.3 percent of the infected women.

Conclusions Among female military recruits, the prevalence of chlamydial infection is high. A control program that screens female recruits who are 25 years old or younger with urine DNA-amplification assays has the potential to reduce infection, transmission, and the sequelae of chlamydial infection. (N Engl J Med 1998;339:739-44.)

MORE than 4 million urogenital *Chlamydia trachomatis* infections occur in the United States annually.[1,2] They occur in young, sexually active persons from all socioeconomic groups, with prevalence ranging from 5 percent to 20 percent.[3,4] Women, especially, bear the burden of disease, with consequences of genital infections ranging from pelvic inflammatory disease to ectopic pregnancy and infertility.[1,5] These sequelae are associated with a large economic burden.[6,7] Because up to 80 percent of infected women are asymptomatic and therefore do not seek medical care, screening of young, sexually active women has been recommended.[1,8] In the past, screening for *C. trachomatis* infections in women has been limited by the need for access to a medical clinic and a pelvic examination. However, *C. trachomatis* infections can now be detected with high sensitivity (85 to 95 percent) and specificity with DNA-amplification assays performed on urine specimens,[9-14] allowing cost-effective screening of large numbers of women in nonclinic settings.[15]

Few studies of the prevalence of chlamydial infection in U.S. military populations have been published, and there have been no studies using DNA-amplification techniques among women not seeking health care.[16-20] Because adolescents have the highest prevalence of disease and most military recruits are young, we conducted a large prevalence study and risk-factor analysis of female recruits from throughout the United States who began basic training at Fort Jackson, South Carolina. We performed this study to determine the extent of infection, assess the feasibility of screening urine specimens for *C. trachomatis* by the ligase chain reaction, and assess which epidemiologic correlates would be useful for implementing an effective chlamydia-control program for female recruits.

METHODS

Population and Specimens

All female Army recruits who were present on Sundays between January 1996 and December 1997 at the Physical Examination Section, Reception Battalion, Fort Jackson, South Carolina, were invited to participate in this study. The study was approved by the institutional review boards of Johns Hopkins University and Fort Jackson (Eisenhower Army Medical Center, Fort Gordon, Ga.), as well as the Human Subjects Research Review Board of the U.S. Army Surgeon General. Of the 16,593 recruits approached, 13,223 (79.7 percent) volunteered to participate in the study and were given a briefing about the study as well as an educational briefing about chlamydial infections by the civilian research nurse.

All subjects signed an informed-consent form and completed a questionnaire regarding demographic information, home state,

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and sexual history. The data instrument was a two-sided scannable form (Scantron, Tustin, Calif.). To determine the similarity of the study subjects and those who chose not to participate in the study with regard to demographic characteristics and sexual history, 823 of the 3370 women who did not volunteer were invited to fill out an anonymous questionnaire. Nonvolunteers were asked to fill out a questionnaire only during the first week of each month.

Each volunteer was instructed to collect 20 to 30 ml of first-catch urine (the first part of the urine stream). A unique study number was assigned to each volunteer. All urine specimens, consent forms, and questionnaires were shipped to the Johns Hopkins University chlamydia laboratory. Urine specimens were kept at 4°C until processed, within 48 hours.

Laboratory Procedures and Treatment

Urine specimens were processed and tested by the ligase chain reaction (Abbott Laboratories, Abbott Park, Ill.) for chlamydial DNA according to the manufacturer's directions. Each week a list of infected subjects was sent to the research nurse. The infected subjects were contacted and treated at the Troop Medical Clinic at Fort Jackson by directly observed therapy with a single 1-g dose of azithromycin. The subjects were also tested for coexisting sexually transmitted diseases. The sensitivity and specificity of the ligase chain reaction in urine specimens as compared with cervical culture for chlamydia had been previously determined to be 88.6 percent and 99.7 percent, respectively, in another military population.[14]

Statistical Analysis

Questionnaire forms were scanned into a data base (dBASE III Plus, Borland International, Spring Valley, Calif.). The results of the ligase chain reaction, demographic information, and risk-factor information were analyzed as dichotomous variables with the chi-square test. Univariate and multivariate logistic-regression analysis for factors associated with chlamydial infection was performed with Intercooled Stata software (version 4.0, Stata, College Station, Tex.). All independent variables were entered into the model, and a two-sided P value of less than 0.05 was considered to indicate statistical significance. The 95 percent confidence interval for the prevalence value for recruits from each state was calculated with Stata software. A one-way analysis of variance was performed to assess the degree of significance of differences in prevalence between states.

RESULTS

Characteristics of the Subjects

Of 13,223 subjects presenting at the Physical Examination Section on Sundays from January 1996 through December 1997, 19 could not be evaluated because of missing data or insufficient urine. The median age of the 13,204 who could be evaluated was 21 years (range, 17 to 39); 87.9 percent (11,603) were 25 years old or younger (Table 1). Fifty-one percent of the women were white, 35.9 percent were black, and 13.1 percent were of other races. For the entire population, the prevalence of *C. trachomatis* infection according to the urine ligase chain reaction was 9.2 percent.

On the questionnaire, 93.1 percent of the subjects reported having ever had vaginal sex, 26.7 percent having had more than one sex partner in the previous 90 days, and 31.4 percent having had a new sex partner in the previous 90 days. Only 16.9 percent reported that their partners always used condoms. A history of chlamydial infection was reported by 9.1 percent of the subjects, gonorrhea by 3.3 percent, syphilis by 0.6 percent, and trichomonas infection by 4.6 percent. Of the volunteers who reported having had no vaginal sex, 1.4 percent (13 of 914) were chlamydia-positive, and of those who reported that their partners always used condoms, 8.4 percent (177 of 2115) were chlamydia-positive.

Of the 823 nonvolunteer recruits who filled out a questionnaire anonymously, 203 (24.7 percent) did not provide their ages and were dropped from the analysis. The mean age of the remaining nonvolunteer recruits was 21 years (range, 17 to 36); 51.3 percent were white, and 31.9 percent were black. The mean age and the racial distribution of these recruits were not significantly different from those of the volunteers. Only 66.9 percent reported having had vaginal sex, as compared with 93.1 percent of the volunteers ($P<0.001$). This group differed significantly from the volunteers in four variables, even after adjustment for whether the women reported having had vaginal sex: only 4.0 percent reported prior chlamydial infections ($P=0.013$), 18.2 percent had had a new sex partner in the previous 90 days ($P=0.002$), 20.1 percent had partners who consistently used condoms ($P<0.001$), and 90.7 percent reported no previous diagnosis of a sexually transmitted disease ($P=0.001$). Of the nonvolunteers, 17.7 percent had had more than one sex partner in the previous 90 days; the proportion of the volunteers who had had more than

TABLE 1. CHARACTERISTICS OF 13,204 FEMALE ARMY RECRUITS SCREENED FOR *CHLAMYDIA TRACHOMATIS*.

CHARACTERISTIC	VALUE
Age — yr	
Median	21
Range	17–39
Race — no. (%)*	
White	6,715 (51.0)
Black	4,733 (35.9)
Other	1,726 (13.1)
Ever had vaginal sex — no. (%)†	12,281 (93.1)
Sexual history in previous 90 days — no. (%)	
More than one partner‡	3,478 (26.7)
New partner§	4,076 (31.4)
Partner always used condoms¶	2,115 (16.9)
Previous diagnosis of sexually transmitted disease — no. (%)	
Chlamydia trachomatis	1,206 (9.1)
Neisseria gonorrhoeae	430 (3.3)
Syphilis	74 (0.6)
Trichomonas	611 (4.6)
None	11,372 (86.1)
Chlamydia-positive — no. (%)	1,219 (9.2)

*Data were missing for 30 subjects.

†Data were missing for 9 subjects.

‡For 168 subjects, data were missing or subject did not know answer.

§For 225 subjects, data were missing or subject did not know answer.

¶For 684 subjects, data were missing or subject did not know answer.

one sex partner in the previous 90 days was similar after adjustment for vaginal sex (P=0.189).

Prevalence of Infection

The age-specific prevalence of *C. trachomatis* infection among the 13,204 volunteers is shown in Figure 1. The highest prevalence of chlamydial infection (12.2 percent) was among 17-year-olds. The prevalence declined sharply with increasing age, to below 5 percent for women over 25 years of age. For further analysis, the youngest age groups (17 to 25 years) were combined into a category called "young." The prevalence in this group was 10.0 percent (1162 of 11,603). In the older-age category (26 to 39 years), the prevalence was 3.6 percent (57 of 1601). The prevalence was 5.5 percent (369 of 6715) for whites, 14.9 percent (707 of 4733) for blacks, and 8.1 percent (143 of 1756) for other races.

Univariate Analysis

Univariate analysis identified 10 variables significantly associated with chlamydial infection: young age (17 to 25 years), black race, race other than white or black, ever having had vaginal sex, having had more than one sex partner in the previous 90 days, having had a new sex partner in the previous 90 days, having had a partner who did not always use condoms in the previous 90 days, a prior diagnosis of gonorrhea, a prior diagnosis of trichomonas, and a history of any sexually transmitted disease (Table 2). A prior diagnosis of chlamydia or syphilis was not significantly associated with being positive for chlamydial infection.

Multivariate Analysis

In the complete multivariate model, having had vaginal sex, an age of 25 years or less, black race, having had more than one sex partner in the previous 90 days, having had a new sex partner in the previous 90 days, having had a partner who did not always use condoms in the previous 90 days, and a history of any sexually transmitted disease were independent predictors of chlamydial infection (Table 3).

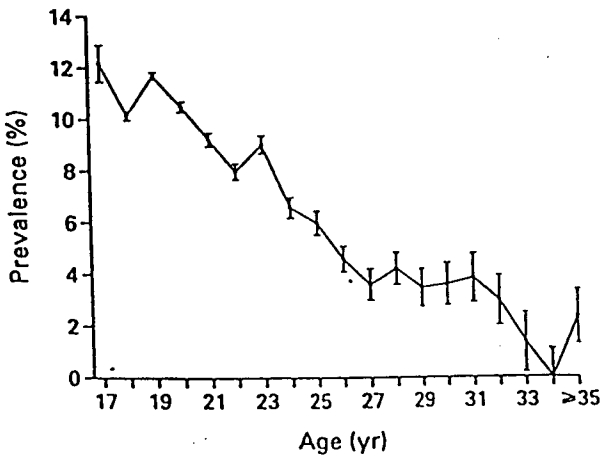

Figure 1. Mean (±SE) Age-Specific Prevalence of Chlamydial Infection among 13,204 Female Army Recruits, According to Ligase-Chain-Reaction Assays of Urine Specimens.

Strategies for Selective Screening

A screening strategy involving all variables identified as independent predictors would require that 100 percent of the population be tested and would detect 100 percent of the positive subjects. In this model, the magnitude of risk associated with having had a new sex partner might vary according to race. For the purpose of a screening program, this would not alter the proportion of the population tested or the percentage of positive subjects detected with this model. Because screening on the basis of race would probably be viewed as inequitable, a strategy excluding race was examined. According to this strategy,

TABLE 2. UNIVARIATE ANALYSIS OF FACTORS ASSOCIATED WITH CHLAMYDIAL INFECTION IN FEMALE ARMY RECRUITS.*

RISK FACTOR	NO. OF RECRUITS	PREVALENCE OF INFECTION		
		RISK FACTOR PRESENT	RISK FACTOR ABSENT	ODDS RATIO (95% CI)
Age ≤25 yr	11,603	10.0	3.6	3.0 (2.3–4.0)
Black race†	4,733	14.9	5.5	3.0 (2.7–3.5)
Other (nonwhite, nonblack) race†	1,726	8.1	5.5	1.5 (1.2–1.9)
Having ever had vaginal sex	12,281	9.8	1.4	7.5 (4.4–13.1)
Having had >1 sex partner in previous 90 days‡	3,478	13.5	7.7	1.9 (1.7–2.1)
Having had a new sex partner in previous 90 days§	4,076	12.4	7.8	1.7 (1.5–1.9)
Having had a partner who did not always use condoms in previous 90 days¶	10,405	9.8	NA	1.2 (1.0–1.4)
Condom use unknown¶	418	5.0	NA	0.6 (0.4–0.9)
Data on condom use missing¶	266	1.5	NA	0.2 (0.1–0.5)
Previous diagnosis of *Neisseria gonorrhoeae*	430	12.3	9.1	1.4 (1.0–1.9)
Previous diagnosis of trichomonas	611	11.6	9.1	1.3 (1.0–1.7)
History of any sexually transmitted disease	1,828	10.5	9.0	1.2 (1.0–1.4)

*CI denotes confidence interval, and NA not available.

†The reference group consisted of the white subjects.

‡The variable is dichotomized: the reference group consisted of the subjects who did not have >1 sex partner, who answered that they did not know, or for whom data were missing.

§The variable is dichotomized: the reference group consisted of the subjects who did not have a new sex partner, who answered that they did not know, or for whom data were missing.

¶The variable is dichotomized: the reference group consisted of the subjects who had a partner who always used condoms.

TABLE 3. MULTIVARIATE ANALYSIS OF FACTORS INDEPENDENTLY ASSOCIATED WITH CHLAMYDIAL INFECTION IN FEMALE ARMY RECRUITS.

RISK FACTOR	ODDS RATIO (95% CI)*
Age ≤25 yr	3.0 (2.3–4.0)
Black race†	3.4 (2.9–3.8)
Other (nonwhite, nonblack) race†	1.7 (1.4–2.1)
Having ever had vaginal sex	5.9 (3.2–10.6)
Having had >1 sex partner in previous 90 days‡	1.4 (1.2–1.7)
Having had a new sex partner in previous 90 days§	1.3 (1.1–1.6)
Having had a partner who did not always use condoms in previous 90 days¶	1.4 (1.1–1.6)
Having ever had a sexually transmitted disease	1.2 (1.0–1.4)

*CI denotes confidence interval.

†The reference group consisted of the white subjects.

‡The reference group consisted of the subjects who did not have >1 sex partner, who answered that they did not know, or for whom data were missing.

§The reference group consisted of the subjects who did not have a new sex partner, who answered that they did not know, or for whom data were missing.

¶The reference group consisted of the subjects who had a partner who always used condoms.

recruits would be tested if they were 25 years of age or less or if they reported on a questionnaire having had more than one sex partner or a new sex partner in the previous 90 days, having had a partner who did not use condoms in the previous 90 days, or having a history of sexually transmitted disease. Screening according to these criteria would still require testing 100 percent of the population. If a questionnaire could be avoided and young age (25 years or less) alone was the screening criterion, 87.9 percent (11,603 of 13,204) of the population would need to be tested and 95.3 percent (1162 of 1219) of the positive subjects would be identified.

Geographic Variation in Prevalence

There was considerable variation in the prevalence of chlamydial infection according to the state of origin of the recruits ($F<0.001$ by one-way analysis of variance). The prevalence was more than 15 percent for recruits from South Carolina, Georgia, Alabama, Louisiana, and Mississippi. For New Jersey, North Carolina, Kentucky, Texas, Oklahoma, and Arkansas, the prevalence was 10 to 15 percent, and for 17 other states and Puerto Rico, it was 5 to 10 percent. For five states (Washington, Oregon, Minnesota, Arizona, and Massachusetts), the prevalence was less than 5 percent. Fewer than 100 recruits were tested from each of 17 states, 3 territories, and the District of Columbia, and prevalence figures from these areas were therefore not included in the analysis. The prevalence for the five states with the highest prevalence and the five states with the lowest prevalence differed significantly, since the 95 percent confidence intervals for prevalence did not overlap.

DISCUSSION

Although the diagnosis and treatment of sexually transmitted diseases has always presented a challenge, there has been no routine screening of recruits for chlamydial infections at entry into the U.S. Army.[21] Because most chlamydial infections are asymptomatic in women and because the sequelae of disease present a severe and costly burden, screening women at entry into the Army is an appropriate way to identify infections early and to explore opportunities for a control program.[1,6,7,22]

Civilian chlamydia-control programs have sought to identify criteria for selective screening.[23-27] Most of these control programs have used diagnostic assays that require pelvic examinations and cervical specimens.[25] However, it has recently been shown that testing urine specimens by DNA-amplification techniques is cost effective for screening large numbers of persons in different settings.[15,28] We used this new technique to determine the prevalence of chlamydia and to identify screening criteria for a program to control chlamydia in the military.[10,12,14] Collection of urine specimens in this study was highly acceptable and easily implemented.

Using the ligase chain reaction with urine samples, we found a high prevalence of *C. trachomatis* infection (9.2 percent). This prevalence was higher than that observed in family-planning clinics[28] but not as high as that reported in some adolescent health clinics.[29,30] Our data agree with those from previous studies of chlamydial infections in Army women, in which prevalence rates ranged from 8.2 percent to 9.8 percent.[17,18] In one large, community-based screening study, the overall prevalence of chlamydia in young women was 8.6 percent, as detected by the urine ligase chain reaction, a prevalence similar to that found in our study.[31] Because our population was not clinic-based and was not made up of women seeking health care, the finding of such a high prevalence in these women warrants the institution of a control program for the routine identification and treatment of chlamydial infections in order to prevent sequelae and transmission to sex partners.[8]

The study population consisted of a young, sexually active group of female recruits with sexual risk factors known to be associated with chlamydial infection.[25] Although 9.1 percent of the subjects reported having had chlamydial infection in the past, this factor was not associated with the risk of current infection. The highest prevalence was observed among 17-year-olds. This prevalence is similar to comparable age-specific rates in other studies, confirming that young age is associated with chlamydial infection.[28,31] In our study, young age was associated with being chlamydia-positive in both univariate and multivariate analyses (odds ratio, 3.0). In order to include more positive subjects, we used an age cutoff of 25 years, which allowed the detection of 95.3 per-

ent of the chlamydial infections. Other studies have supported age-based screening for chlamydia.[27,31,32]

Thus, for this group of female recruits coming from a civilian background, who were tested within three days of starting basic training, young age alone can be recommended as a single indicator of who should be tested for chlamydial infection. Other models considered in this study offered high sensitivity, but the models were more complex and required valid sexual-risk histories. We documented 13 chlamydial infections (prevalence, 1.4 percent) among 914 recruits who denied being sexually active, as well as chlamydial infections in 8.4 percent of those who reported that their partners consistently used condoms. These figures indicate that self-reported sexual-risk histories are not always valid.[33] The lower prevalence of chlamydial infection among recruits for whom the data on condom use were missing, or who indicated on their questionnaires that they did not know whether their partners always used condoms, may be due to lack of sexual activity, because 58.6 percent of the 684 recruits in these categories reported that they had never had vaginal sex. There is a fixed laboratory budget available for population screening in the Army. Young age is the simplest, least expensive, and most easily documented risk factor on which to base a recommendation for a screening program, as well as being highly sensitive. Alternatively, since the use of age as a selective screening criterion would have missed 4.7 percent of the infections, universal screening might be more cost effective from a societal perspective, and future studies of cost effectiveness are warranted.[28]

This was one of the largest programs for screening young, sexually active subjects that was not clinic-based and whose results were derived from urine DNA-amplification assays. The geographic variation in prevalence was striking. From more than 15 percent in the five states with the highest prevalence to less than 5 percent in the five states with the lowest, these differences may reflect the levels of disease burden in certain states. These regional variations also appear to reflect regional differences in chlamydial disease, as reported by the Centers for Disease Control and Prevention.[34,35] For example, the prevalence in North Carolina reportedly varied from 10 percent to 17 percent.[35] The prevalence is lower in regions such as Wisconsin and Washington State, where clinic-based chlamydia-control programs are in place and where declining rates of prevalence of chlamydia have been reported.[26,27,32,36] In our study, the prevalence was 11.3 percent for North Carolina and 3.8 percent for Washington State. Our data imply that chlamydial infection remains common in young women across the United States. With a volunteer rate of percent among women who were approached and representation from 50 states and 4 territories, our study had a wide geographic sampling.

One limitation of our study is that it is not known whether the prevalence of risk factors for chlamydial infection differs between young women who decide to join the military and those who do not. However, the demographic and sexual risk-factor characteristics of our subjects appear to be similar to those of other regional and clinic-based populations,[25] as well as those from a large, community-based study.[31] An additional limitation is that the nonvolunteers in our study differed from the volunteers with regard to sexual risk factors for chlamydia. However, the nonvolunteers represented a group who were mostly sexually active, who had had new sex partners in the previous 90 days, and whose partners did not use condoms. Thus, their risk of chlamydial infection may have been as high as that of the subjects in our study.

Although amplified-DNA tests are more expensive than traditional nonculture tests, the savings associated with not having to have a clinician collect specimens from a pelvic examination and the advantages of being able to use urine as a diagnostic specimen may outweigh the extra cost of the test.[15] In addition, it has been demonstrated that amplified-DNA testing of urine specimens is cost effective, and treating chlamydial infections prevents serious complications such as pelvic inflammatory disease, ectopic pregnancy, and infertility.[15,28,37]

In conclusion, our study indicates that with the limited funding available at present, young age (25 years or less) would be the best criterion on which to base a screening program using amplified-DNA testing of urine for female Army recruits and perhaps for other young women. Institution of such a control program has the potential to reduce drastically the burden of chlamydial disease in the U.S. Army and to prevent morbidity due to these infections.[37]

Supported by a grant (DAMD17-95-1-5064) from the Department of the Army.

The opinions expressed in this article are those of the authors and are not necessarily endorsed by the U.S. Army or the Department of Defense.

We are indebted to Dr. Daniel Scharfstein, Mary Sheppard, Dr. Guillermo Madico, and Dr. Anne Rompalo for statistical assistance; to Kathryn Kacena for data entry; to Diane Perkins, Sandra Leister, Dien Pham, and Graciela Jaschek for performance of the laboratory tests; to Lt. Col. Cynthia Dodd, Lt. Col. (ret.) Delois Daniels, and Kimberly Riley for treatment of infected women and processing of specimens; and to Patricia Buist for assistance in the preparation of the manuscript.

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JOURNAL OF CLINICAL MICROBIOLOGY, May 1998, p. 1300–1304
0095-1137/98/$04.00+0

Vol. 36, No. 5

Use of Ligase Chain Reaction with Urine versus Cervical Culture for Detection of *Chlamydia trachomatis* in an Asymptomatic Military Population of Pregnant and Nonpregnant Females Attending Papanicolaou Smear Clinics

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Received 13 November 1997/Returned for modification 27 January 1998/Accepted 16 February 1998

Ligase chain reaction (LCR) (Abbott Laboratories, Abbott Park, Ill.) with first-catch urine specimens was used to detect *Chlamydia trachomatis* infections in 465 asymptomatic military women attending clinics for routine Papanicolaou smear tests. Results were compared to results of cervical culture to determine the sensitivity of the urine LCR and the possible presence of inhibitors of amplification in pregnant and nonpregnant women. Discrepant results for LCR and culture were resolved by direct fluorescent antibody staining of culture sediments, two different PCR assays, and LCR for the outer membrane protein 1 gene. The prevalence of *Chlamydia* in specimens by urine LCR was 7.3% compared to 5% by culture. For 434 women with matching specimens, there were 11 more specimens positive by LCR than were positive by culture, of which all but one were determined to be true positives. There were four culture-positive, LCR-negative specimens, all from nonpregnant women. The sensitivity, specificity, and positive and negative predictive values of urine LCR after discrepant results were resolved were 88.6, 99.7, 96.9, and 99.0%, respectively. The sensitivity of culture was 71.4%. From the 148 pregnant women (prevalence by LCR, 6.8%), there were no patients who were cervical culture positive and urine LCR negative to indicate the presence in pregnant women of inhibitors of LCR. Additionally, a subset of 55 of the LCR-negative frozen urine specimens from pregnant women that had been previously processed in LCR buffer were inoculated with 5 cell culture inclusion forming units of *C. trachomatis* each and retested by LCR; all tested positive, indicating the absence of inhibitors of LCR in urine from these pregnant women. The use of LCR testing of urine specimens from asymptomatic women, whether pregnant or not, offers a sensitive and easy method to detect *C. trachomatis* infection in women.

Approximately 4 million *Chlamydia trachomatis* urogenital infections occur in the United States annually, and more than 50 million cases occur worldwide (7, 28). Unfortunately, symptoms are often mild or absent among infected men and women, leaving a large reservoir of infected persons to continue transmission to new sex partners (29). Chlamydial infections occur primarily among young sexually active persons. A high prevalence is common to all socioeconomic groups and may range from 5 to 20% in various groups of young adults (32, 33). Because of the high probability of progression of asymptomatic disease to serious sequelae, it has been recommended that individuals at risk for chlamydial infections be screened, especially women who are vulnerable to the serious consequences of genital infections, such as pelvic inflammatory disease, ectopic pregnancy, and tubal infertility (7, 11). Urine can now be used to detect chlamydial infections in women by ligase chain reaction (LCR) (2, 8, 14, 20, 31, 34), which with its easily obtained specimen is a cost-effective method for screening programs for asymptomatic women (16). Because asymptomatic military populations have not been studied widely with regard to chlamydial infections (4, 6, 10, 21, 26, 27) and because the sensitivity of the urine LCR assay has been reported to be low for samples from pregnant women due to the presence of inhibitors to amplification (18), we compared urine LCR to cervical culture for the detection of *C. trachomatis* in asymptomatic women attending clinics for routine Papanicolaou (PAP) smear tests.

MATERIALS AND METHODS

Populations and specimens. Military women (n = 480) attending clinics for a routine PAP smear test volunteered for a study to compare urine LCR tests to cervical cultures for the detection of *C. trachomatis* infections. The volunteer rate of the women approached by the civilian research nurse was 71%. The study was approved by the Institutional Review Boards of The Johns Hopkins University, the U.S. Army Medical Research Material Command, Fort Detrick, Fredrick, Md., and Womack Army Medical Center, Fort Bragg, N.C. Of 480 women enrolled, 465 provided a urine specimen. All subjects completed a questionnaire for demographic information and behavioral risk factors for sexually transmitted diseases. The data instrument was a one-page, two-sided scanable bubble form (Scanntron Corporation, Tustin, Calif.). During the pelvic examination, an endocervical swab was obtained by the attending clinician at the PAP smear clinic, who recorded clinical signs and symptoms on the data form. Culture swabs were placed into 2-sucrose-phosphate chlamydia transport medium. Commercial transport medium was replaced with in-house transport medium after 1 month of the study due to some toxicity of the former to tissue culture cells. Specimens were stored appropriately (4°C for urine specimens and −70°C for cultures) until shipping of the urine specimens at 4°C and cultures at −70°C. Shipments were made to ensure arrival at the laboratory within 4 days of collection. All specimens, consent forms, and data forms were shipped to Johns Hopkins Chlamydia Research Laboratory.

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Laboratory procedures. Urine specimens were processed and tested by LCR (Abbott Laboratories, Abbott Park, Ill.) according to the manufacturer's instructions. Briefly, 1 ml of urine was centrifuged at 15,000 × *g* for 15 min. After the supernatant was removed, 1 ml of urine buffer was added to the pellet and the mixture was vortexed. After being heated at 97°C for 15 min, specimens were cooled and 100 μl of each specimen was added to an LCR unit dose tube. An appropriate chlamydia-positive control was included for the processing steps for each group of specimens. Additionally, two negative controls and two positive calibrator controls supplied by the manufacturer were used for each LCR assay run. After the amplification step in the automated thermocycler, unit dose tubes containing the specimens and controls were transferred to the automated enzyme immunoassay machine for the detection of amplified products. Tubes containing the amplified products were never opened; the automated enzyme immunoassay process sampled tubes by piercing the tops of the unit dose tubes, which prevented amplicon contamination. In order to prevent other sources of contamination, specimens were processed in a designated room separate from the room used to amplify and detect specimens. Gloves were frequently changed and aerosol-barrier pipette tips and dedicated pipettors were used. Strict quality-control measures such as machine maintenance checks, daily cleaning of laboratory areas and equipment with bleach, and area swipe tests to monitor amplicon contamination were employed.

Culture specimens were stored frozen at −70°C for up to 3 days. Cultures were done in 96-well microwell plates in McCoy cells by standard methods (12). Tissue cultures were stained with genus-specific fluorescein-conjugated antibody (Kallested, Chaska, Minn.) and species-specific antibody (Boehringer Mannheim/Syva, San Jose, Calif.). Stained cultures were read for the presence of chlamydial inclusion bodies with an epifluorescence microscope.

Discrepancy analysis was done for any sample with discordant results between culture and LCR. A sample that was positive by culture and negative by LCR was considered to be a true positive, but the discrepancy was investigated for the presence of inhibitors to amplification by LCR. The urine LCR was repeated from the originally processed specimen and repeated again after diluting the processed specimen 1:10 in urine LCR buffer to check for the presence of inhibitors in the specimen. (Dilution has been shown to sometimes decrease the concentration of the inhibitor enough to allow a true-positive specimen to be amplified.) Additionally, PCR (Roche Diagnostic Systems, Branchberg, N.J.) was done on an archived aliquot of frozen urine and another LCR was done for a different DNA target, the outer membrane protein 1 (OMP-1) gene. For specimens that were positive by LCR and negative by culture, the culture specimen transport sediment was stained by direct fluorescent antibody (DFA) (Boehringer Mannheim/Syva) for chlamydial elementary bodies. PCR also was done on the specimens from the culture transport vials. In addition, PCR was done on the archived urine and an LCR for the OMP-1 gene was done on the previously processed (buffered) urine specimen. Specimens that were positive by one or more of the ancillary tests were considered true positives. An LCR-positive urine specimen which could not be confirmed by another test was considered to be a false positive.

Testing of urine specimens from pregnant women. A subset of all available (n = 55) previously processed (buffered) LCR-negative urine specimens that were from pregnant women were inoculated with 5 inclusion forming units of *C. trachomatis* and retested by LCR to check for the presence of inhibitors. Additionally, 65 archived LCR-negative unprocessed urine specimens that were available from pregnant women were tested by a research internal control assay to evaluate the presence of inhibitors (9). This assay tested for the ability to amplify an extraneous sequence of DNA which was added as an internal control to the specimen. The assay contained primers for the extraneous DNA internal control as well as the primers for the organism of interest. A positive amplification of the internal control indicated that the specimen contained no inhibitors to the amplification process, while a negative result indicated that the specimen contained something which inhibited the amplification process.

Data analysis. The data from the questionnaire forms were scanned into a data set (D-base III Plus; Ashton Tate, Borland International, Spring Valley, Calif.), and LCR results, demographics, and risk factor information were analyzed by the chi-square test, Fisher's tests of exactness, and univariate analysis (Intercooled Stata, version 4.0; Stata Corporation, College Station, Tex.).

TABLE 1. Characteristics of military women screened for *C. trachomatis* at Fort Bragg, N.C.

Variable	No. of women (n = 480)	%
Median age, yr (range)[a]	25 (19–47)	
Ethnicity[b]		
White	181	37.7
African-American	244	50.8
Other (American Indian, Alaskan, or Asian Pacific)	52	10.8
Military category[c]		
Enlisted personnel	439	91.5
Officer	36	7.5
Reason for clinic visit[c]		
Sex partner of infected individual	1	0.2
Complaint of symptoms	1	0.2
Screening	470	97.8
Other	4	0.8
Clinical presentation[d]		
Mucopus	1	0.2
Cervicitis	5	1.0
Ectopy	5	1.0
Cervical motion tenderness	3	0.6
Friability	39	8.1
Pregnant	148	30.8
Normal exam	348	72.5
Sexual history (past 90 days)		
More than one sex partner	73	15.2
New sex partner	54	11.3
Consistent condom use	51	10.6
Inconsistent condom use	425	88.5
Previous diagnosis[e]		
N. gonorrhoeae	20	4.2
C. trachomatis	86	17.9
Syphilis	5	1.0
Trichomonas	41	8.5
None	348	72.5
Chlamydia-positive urine LCR[f]	34	7.3
Chlamydia-positive culture[g]	24	5.3

[a] Data missing for eight women (1.7%).
[b] Data missing for three women (0.6%).
[c] Data missing for five women (1.0%).
[d] Data missing for 27 women (5.6%).
[e] Data missing for two women (0.4%).
[f] Urine specimen for LCR missing for 15 women.
[g] Cervical specimens for culture missing for 21 women and 10 toxic specimens collected.

RESULTS

Patient characteristics. Among the 480 women enrolled, only 1 woman had reported mild symptoms and the remainder were asymptomatic. Approximately half (55.2%) were 25 years or younger, and 50.8% were African-American. Over 90% were enlisted personnel, 98.3% reported vaginal sex, 11.3% had a new sex partner in the previous 90 days, 15.2% had more than one sex partner in the previous 90 days, 88.5% reported inconsistent condom use, and 30.8% were pregnant (Table 1). Reasons for clinic visit, clinical presentation, and sexual risk history are presented in Table 1. Of the 465 women who provided a urine specimen, the overall prevalence for chlamydia infection by LCR was 7.3%. The prevalences of infection for other categories based on LCR included 11.0% for women ≤25 years of age, 8.9% for African-American women, and 6.8% for pregnant women. By risk category the prevalences were 15.1% for those with a new sex partner in the previous 90 days, 10.3% for those with more than one sex partner in the previous 90 days, 7.5% for those with inconsistent condom use, 7.4% for those reporting vaginal sex, and 3.6% for those with a prior chlamydial infection.

In univariate analysis only young age (≤25 years) (odds ratio [OR], 4.23; 95% confidence interval [CI], 1.72 to 10.43) and a new sex partner (OR, 2.61; 95% CI, 1.11 to 6.1) were predictors of chlamydial infection (Table 2). However, when we controlled for age, a new sex partner was no longer significant.

Comparison of urine LCR to cervical culture. Of the 465 women, 31 women did not have matched culture specimen results. Ten specimens were toxic for tissue culture and no cervical cultures were collected from 21 women, leaving 434 matched specimens for comparison. After the use of the commercial chlamydia transport buffer was stopped and the in-

TABLE 2. Univariate analysis of results relative to factors associated with positive urine LCRs for military women attending PAP smear clinics

Factor[a]	% with a positive LCR		OR (95% CI)	P
	Factor absent	Factor present		
Age ≤25 yr (254)	2.8	11.0	4.2 (1.72, 10.43)	0.002
African-American (233)	6.8	8.6	1.3 (0.61, 2.7)	0.501
Pregnant (142)	7.4	7.0	0.94 (0.44, 2.03)	0.882
Normal pelvic exam (275)	12.5	6.6	0.49 (0.18, 1.31)	0.154
Prior diagnosis of STD[b] (127)	8.3	3.9	0.45 (0.17, 1.2)	0.110
Having had more than one sex partner in last 90 days (68)	6.8	10.3	1.6 (1.53, 3.73)	0.316
Having had a new sex partner in last 90 days (53)	6.4	15.1	2.6 (1.11, 6.10)	0.027[c]

[a] Numbers in parentheses represent numbers of individuals with the factor present (n = 465).
[b] STD, sexually transmitted disease (chlamydia, gonorrhea, syphilis, or trichomonas).
[c] A new sex partner was not significant when we controlled for age.

house 2-sucrose-phosphate medium was used, no further specimens toxic to tissue culture were observed. Among the 31 specimens without matched results, there were two LCR-positive urine specimens for which a matching cervical culture was not collected.

From the 434 matched specimens, 32 (7.4%) were LCR positive, of which 31 (7.3%) were confirmed as true positives (Table 3). There were 21 LCR-positive, culture-positive specimens. Four patients had urine-LCR-negative, cervical-culture-positive specimens. Discrepancy analysis of these LCR-negative, culture-positive specimens demonstrated that one was positive in the repeat LCR assay and was OMP-1 LCR positive, one had a negative value which was close to the cutoff value for a positive result and was PCR positive when the archived frozen urine was tested, one had a culture transport specimen that was PCR positive, and the results of one could not be confirmed by any of the ancillary tests, including repeat culture. The initial LCR-negative results from these four urine specimens were all considered to be false negatives.

There were 11 specimens that were LCR positive and culture negative, 10 of which could be confirmed as true-positive specimens (Table 4). Five were DFA positive, six were urine PCR positive, seven were culture PCR positive, and eight were OMP-1 LCR positive. Thus, all but one of these LCR-positive specimens were confirmed as true positives by at least one or more additional assays. After resolution of the discrepant results, the sensitivity, specificity, and positive and negative predictive values of urine LCR were 88.6, 99.7, 96.9, and 99.0%, respectively (Table 3), and the sensitivity of culture was 71.4%.

LCR of urine of pregnant women. There were 148 urine specimens from pregnant women. The prevalence of chlamydia infection by LCR for the pregnant women was 6.8%, and that for the nonpregnant women was 7.8%. There were no culture-positive, LCR-negative results from pregnant women which could have indicated the presence of LCR inhibitors. All four of the culture-positive, LCR-negative specimens were from women who were not pregnant. In addition, a subset of 55 LCR-negative urine specimens, previously processed in LCR buffer and frozen, which were from pregnant women and were inoculated with chlamydia and retested by LCR were all LCR positive, indicating the lack of inhibitors. Of the 65 available archived urine specimens from pregnant women which were LCR negative and tested in the internal control assay, there were 3 (4.6%) that exhibited inhibition based on a negative value for amplification of the internal control.

DISCUSSION

Chlamydia infections were of a higher prevalence than expected from these asymptomatic military women attending a clinic for a routine PAP smear test. An LCR prevalence of 7.3% underscores the necessity for the recommendation to screen all sexually active young women when they are attending a routine health care clinic (7). The high prevalence of 11.0% for those ≤25 years of age confirm the result of studies of others that young age is a significant risk factor for chlamydial infections (13, 17, 22). These results indicate the need

TABLE 3. Comparison of urine LCR to cervical culture for *C. trachomatis* in military women attending PAP smear clinics

Test	Result	No. of women[a] with test result (%)	Resolved patient infection status[b]	
			Positive	Negative
Cervical culture	Positive	25 (5.8)	25	0
	Negative	409 (94.2)	10	399
Urine LCR[c]	Positive	32 (7.4)	31	1
	Negative	402 (92.6)	4	398

[a] Four hundred eighty women enrolled; 434 had matching specimens.
[b] Resolved patient infection status was defined as the resolved status of a patient with a positive culture or with a urine specimen positive by two tests (LCR, DFA staining, PCR OMP-1 gene, PCR plasmid gene, and LCR OMP-1).
[c] After discrepant results were resolved, sensitivity was 88.6%, specificity was 99.7%, and positive and negative predictive values were 96.9% and 99.0%, respectively (sensitivity of culture, 71.4%).

TABLE 4. Resolution of urine-LCR-positive and cervical-culture-negative discrepant results for *C. trachomatis* in military women attending PAP smear clinics (n = 11)

Laboratory no.	Test result					Status
	LCR (urine)	DFA[a]	PCR (urine)	PCR (cervix)	LCR for OMP-1 (urine)	
1264	+	−	−	−	+	Confirmed
2407	+	+	+	+	+	Confirmed
3197	+	+	+	+	+	Confirmed
3659	+	−	−	+	−	Confirmed
3891	+	−	−	−	+	Confirmed
5560	+	+	−	+	+	Confirmed
5570	+	−	−	−	−	Unconfirmed
6082	+	−	+	+	+	Confirmed
6280	+	+	+	+	−	Confirmed
6966	+	+	+	+	+	Confirmed
8016	+	−	+	−	+	Confirmed

[a] DFA staining of culture transport vial specimen.

for an ongoing chlamydial control program for such female military personnel as those enrolled in this study. This population demonstrated a high degree of sexual behaviors placing them at risk for sexually transmitted diseases, with 98% being sexually active, 15% having more than one partner, 11% having a new partner in the last 90 days, and 88% using condoms inconsistently. All of these behaviors have been shown by others to be predictive of chlamydial infection (1, 22–24, 36). In the univariate analysis for this study, both young age (prevalence, 11.0%) and having had a new partner (prevalence, 15.1%) reached statistical significance. However, when we controlled for age, a new sex partner was not significant. Young age (≥25 years), which is an easily determined risk factor and which is a nonthreatening question for those women who may be reticent to answer questions about their sexual behavior, appears to be an excellent predictor of chlamydia infection and can be recommended for deciding who should be screened in clinical or outreach situations (13, 17).

Urine LCR performed well in this study of asymptomatic women, with a sensitivity of 88.6%, which is similar to that demonstrated by others for asymptomatic women (87.5%) (2). Compared to cervical culture, which had a sensitivity of 71.4%, LCR detected more infected women. Many reasons can account for the lower culture sensitivity. Not only can the cold chain of transport be interrupted, but the quality of the transport medium is important as well. Initially, a commercially available transport medium was used in this study, which resulted in many (10) toxic tissue culture results. Quality-control assays of the remaining lot of uninoculated transport medium demonstrated that it was toxic to cells in tissue culture. After switching to the use of our own transport medium, which is quality controlled in tissue culture, we observed no further toxicity.

Additionally, the quality of the endocervical specimen, as measured by the presence of columnar epithelial cells, has been shown to play a significant role in the numbers of positive specimens (19, 37). In another study of family-planning clinics in Baltimore, Md., clinicians obtained adequate specimens only 72.3% of the time (37). Thus, inadequate cervical swab specimens could have contributed to the lower sensitivity of culture in our study. Other studies have demonstrated higher sensitivities for urine LCR than cervical culture (2, 5, 8, 20, 31, 34). Sensitivities for cervical culture in these studies has ranged from 45.5 to 46.9% to 55.6 to 65.0% (2, 5, 8, 34). Schachter et al. have demonstrated that the sensitivity of culture for *C. trachomatis* may be increased from 67.1% to 74% by adding a urethral swab culture, which could be indicative that some women may be infected only in the urethra and not the cervix (31). This could help explain the higher number of positives found by urine LCR, presumably reflecting infections from both the cervix and the urethra. Because urine is an easy-to-obtain, noninvasive specimen giving accurate results with LCR, it is ideal for screening asymptomatic individuals who may not be presenting for a pelvic exam or for outreach screening programs.

Although our study enrolled only 148 women who were pregnant, we did not observe any indication of inhibitors in urine specimens, as evidenced by the lack of urine-LCR-negative results when the cervical culture was positive. Although there were four such specimens in this study, they were all from nonpregnant women. Another study has reported a significant problem with inhibitors in urine with use of the LCR test; however, the urine specimens were transported at ambient temperatures, which may have influenced the LCR results (18, 25, 30). The spiking experiment in our study did not demonstrate any inhibitors in the 55 LCR-negative, previously frozen urine specimens from pregnant women. It is possible that freezing and thawing of these processed urine specimens reduced or destroyed some LCR inhibitors. Freezing and thawing reduced the inhibition from 19 to 16% in one study (35). Additionally, the experiment which tested the archived urine of 65 pregnant women demonstrated only three (4.6%) inhibited specimens. This value is of the same order of magnitude as that reported by others for inhibition in urine specimens (2.6 and 1.8%) for amplified testing (3, 15). Most investigators now believe that inhibitors to amplification exist for both urine and cervical specimens (3, 15, 35). A combination of heat treatment (95°C for 10 min) and 10-fold dilution of the processed specimen reduced inhibition of PCR from 19 to 4% in one study (35). The pH of the cervical mucosa was partly correlated with inhibitors (35). Decreased inhibition was found at pH values of ≥7.5. The degree to which inhibitors to amplification influence the prevalence detected by LCR and PCR needs to be further studied. Roche Molecular Systems has addressed this problem by incorporating an internal DNA control amplification and detection assay into their new combination PCR assay for *C. trachomatis* and *Neisseria gonorrhoeae*, which will prove to be a great advance in the diagnostic capability of amplification assays. Specimens exhibiting inhibitors can be diluted or heated and their DNA can be extracted, and tests can be repeated. The use of the internal control will give a greater degree of confidence to the validity of a negative amplification result. Consideration of the use of an internal control should be given for amplification tests in the future. The College of American Pathologists now requires examination of a control to assess the presence of inhibitors in all amplification procedures.

In summary, young sexually active women, including those in the military, should be frequently screened for chlamydia infections. Urine LCR offers an easy and sensitive method to accomplish this, especially for women not presenting for a pelvic examination. It is cost-effective in preventing the expensive sequelae of pelvic inflammatory disease, ectopic pregnancy, and tubal infertility (16).

ACKNOWLEDGMENTS

We thank the study coordinator, Barbara Pare; the research nurses Eleanor Howard, Katy Cline, and Bobbi Jones and the staffs of the Fort Bragg clinical sites for obtaining specimens; the laboratory technicians Graciela Jaschek, Laura Welsh, Dien Pham, Diana Perkins, Sandy Leister, and Kimberly Crotchfeld for performance of laboratory tests and data entry; Kathryn Clark for statistical assistance; and Pat Buist for assistance in manuscript preparation.

Funding for this study was from Department of the Army grant DAMD 17-95-1-5064.

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JOURNAL OF CLINICAL MICROBIOLOGY, Feb. 1998, p. 481–485
0095-1137/98/$04.00+0

Vol. 36, No. 2

Pooling Urine Samples for Ligase Chain Reaction Screening for Genital *Chlamydia trachomatis* Infection in Asymptomatic Women

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Received 23 July 1997/Returned for modification 19 September 1997/Accepted 4 November 1997

The accuracy of pooling urine samples for the detection of genital *Chlamydia trachomatis* infection by ligase chain reaction (LCR) was examined. A model was also developed to determine the number of samples to be pooled for optimal cost savings at various population prevalences. Estimated costs included technician time, laboratory consumables, and assay costs of testing pooled samples and retesting individual specimens from presumptive positive pools. Estimation of population prevalence based on the pooled LCR results was also applied. After individual urine specimens were processed, 568 specimens were pooled by 4 into 142 pools and another 520 specimens were pooled by 10 into 52 pools. For comparison, all 1,088 urine specimens were tested individually. The sample-to-cut-off ratio was lowered from 1.0 to 0.2 for pooled samples, after a pilot study which tested 148 samples pooled by 4 was conducted. The pooling algorithm was 100% (48 of 48) sensitive when samples were pooled by 4 and 98.4% (61 of 62) sensitive when samples were pooled by 10. Although 2.0% (2 of 99) of the negative pools of 4 and 7.1% (1 of 14) of the negative pools of 10 tested presumptive positive, all samples in these presumptive-positive pools were negative when retested individually, making the pooling algorithm 100% specific. In a population with 8% genital *C. trachomatis* prevalence, pooling by four would reduce costs by 39%. The model demonstrated that with a lower prevalence of 2%, pooling eight samples would reduce costs by 59%. Pooling urine samples for detection of *C. trachomatis* by LCR is sensitive, specific, and cost saving compared to testing individual samples.

There are 89.9 million cases of genital *Chlamydia trachomatis* infection every year worldwide (13), 4.5 million of which occur in the United States (4). Although many *C. trachomatis* infections are asymptomatic (16), the sequelae from infection, including pelvic inflammatory disease (PID), and infertility, represent a large burden for populations worldwide. Furthermore, inflammatory sexually transmitted diseases, such as those caused by *C. trachomatis*, increase the risk of both human immunodeficiency virus (HIV) transmission and infection (7, 11). Together, the high percentage of asymptomatic infections, the sequelae of infections, and the increased association with HIV transmission underscore the importance of screening as a necessary intervention to reduce the burden of diseases caused by *C. trachomatis*.

Detection of genital *C. trachomatis* infection by ligase chain reaction (LCR) with first-void urine is a noninvasive, highly sensitive, and highly specific procedure (2, 8). Although the cost of LCR is higher than that of other tests such as direct fluorescent antibody, antigen detection by enzyme immunoassay, and nucleic acid probe tests, LCR is more sensitive and more specific (15, 17). Culture has been considered to be the "gold standard" in the past but costs more and is less sensitive than either LCR or PCR (3, 5, 10, 12, 14).

Pooling serum samples for HIV testing was found to be accurate and has been used to reduce the cost of enzyme-linked immunosorbent assays for detection of antibody to HIV (1, 6). Pooling for HIV testing has been used to develop both population estimates and, in a multiple-step procedure, to determine which individual sample is positive. Pooling has also been applied to the PCR detection of *C. trachomatis* in endocervical and urethral scrapes (9), but in that study the sample size was small. The investigators acknowledged the need for subsequent studies to rule out the possibility of reduced sensitivity by diluting out individual specimens in the pool.

The screening of women at risk for *C. trachomatis* has been recommended by the Institute of Medicine as a cost-effective program which would prevent the high cost of untreated infections which lead to PID (4). As a screening and treatment intervention reduces the prevalence of *C. trachomatis* infection over time, the cost per specimen tested with the pooling protocol algorithm would be further decreased. The reduction in price occurs for two reasons: (i) as prevalence decreases, pooling a greater number of samples increases cost savings and (ii) the samples from fewer pools would test presumptive positive such that fewer samples would be retested individually. Therefore, the cost for finding one case does not increase dramatically as prevalence decreases, as is the case when samples are tested individually.

In this study we examined the accuracy and cost-saving ability of pooling urine specimens for the detection of genital *C. trachomatis* infections by LCR. A cost analysis of the pooling protocol was conducted to determine the number of specimens it would be necessary to pool in order to provide the

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highest cost savings, taking into account the prevalence of infection in the population screened.

MATERIALS AND METHODS

Sample size and parameters. As part of an ongoing study to determine chlamydia prevalence in asymptomatic U.S. Army females with a mean age (± standard deviation [SD]) of 22 (±4 years), urine samples were tested by LCR to ascertain genital *C. trachomatis* infection. A sample of 568 processed urine specimens was pooled by 4 into 142 pools, and 520 specimens were pooled by 10 into 52 pools. Pools were formed by order of consecutive laboratory accession number. All 1,088 pooled urine samples were also tested individually. For all discrepant individual and pool results, both the individual samples and the pools were retested to confirm results.

Urine specimen, collection, preparation and assay setup. Specimen, collection, preparation, and assay setups were performed according to the manufacturer's instructions for the urine-based chlamydia LCR assay (Abbott Laboratories, Abbott Park, Ill.).

Specimens were refrigerated immediately after collection and shipped overnight delivery with wet packs to maintain refrigerator temperature. Specimens were either processed immediately on arrival at the laboratory or refrigerated and processed within 2 days. The total time before processing never exceeded 4 days as per the LCR package insert. Processed refrigerated specimens were amplified the day after processing. Processed urine can be refrigerated or frozen for up to 60 days before testing. We refrigerated our processed specimens for up to 7 days in case retesting was needed.

One milliliter of urine was centrifuged at ≥9,000 × *g* for 15 min (±2 min) at room temperature. The supernatant was removed, and the pellet was resuspended into 1.0 ml of LCR urine specimen resuspension buffer and vortexed. Preparations were then boiled at 97°C (±2°C) for 15 min (±1 min) to extract the DNA and stored at 2 to 8°C for up to 7 days until tested. Processed urine specimens were subsequently tested individually and tested pooled.

When specimens were tested individually, a volume of 100 μl of processed urine specimen was placed into its own LCR chlamydia amplification vial (unit dose). For each pool of four, 25 μl of each of the four processed specimens was placed into a single unit dose. For each pool of 10, 10 μl of each of the ten processed specimens was placed into a single unit dose. The total specimen volume was then 100 μl for each unit dose. Two negative controls, two positive calibrators, and a positive processing control were included in every amplification run in accordance with the manufacturer's instructions.

DNA amplification and detection. Unit dose tubes containing DNA preparations were amplified under the following conditions: 40 cycles of denaturation at 93°C for 1 s, annealing at 59°C for 1 s, extension at 62°C for 1 min, 10 s, and soaking at 25°C in an LCR thermocycler (Abbott Laboratories). Amplified DNA was detected in an LCR-automated machine which performed a particle-based enzyme immunoassay with a fluorescent signal. For individually tested samples, a sample-to-cutoff ratio (S/CO) of ≥1.0 was considered positive, and borderline negative samples (0.80 to 0.99 S/CO) were retested, according to manufacturer's instructions.

Pilot study. Because the volume for each individual urine specimen is decreased in the pooled assay, a pilot study was conducted to determine an appropriate S/CO for the pooled assays. The desired S/CO would detect all positive pools while not detecting most, if not all, negative pools. The pilot study consisted of 148 processed urine samples from the ongoing study of female U.S. Army recruits. The technician, blinded to the individual test results, pooled and tested these 148 samples by four. By lowering the S/CO from 1.0 to 0.2, all of the positive pools were detected (100%) (25 of 25) and only 2.7% (1 of 37) of the negative pools tested presumptive positive. Since all pools which test positive are retested, specificity with the pooling algorithm is 100%, i.e., no different than with testing processed specimens individually.

Cost analysis. A model was developed to determine the pool size that yielded the highest cost savings. The binomial distribution was used to estimate the number of pools that are likely to be positive given a selected pool size and population disease prevalence. Next, the optimal pooling number for a range of disease prevalences was calculated. For a dichotomous outcome (i.e., positive or negative test result for a genital *C. trachomatis* infection), independence was assumed (i.e., the order of the samples received was random with regard to the distribution of the positive or negative samples in the population). The expected percentage of positive pooled assays was determined using the following equation: $s = [(1 - r/n)^c] \times 100\%$, where s is the expected number of positive pools, r is the number of positive samples tested, n is the total number of samples tested, r/n is the prevalence of disease, and c is the number of specimens pooled. This equation accounted for the probability that from 1 to c samples in the pool were positive.

A baseline total cost of $12.76 per individual sample which included $0.36 for laboratory consumables, $3.56 for technician cost, and $8.84 for the LCR assay was used. Laboratory consumables include gloves and supplies used for handling samples. Technician cost was calculated assuming an average of 10 runs per week (i.e., 380 samples), an annual salary of $30,000 with an additional 28% of salary in benefits, and a 69% laboratory or university overhead (i.e., $30,000 × 1.28 × 1.69 = $64,896). The cost of the five controls used for each 19 specimens tested was calculated into the LCR assay cost, in which the base cost per unit dose was $7. A sensitivity analysis was also done first, with the base cost per unit dose ranging from $5 to $15, technician cost set at $3.56, and cost for laboratory consumables set at $0.36 per specimen tested. In the second sensitivity test, the annual salary of the technician ranged from $20,000 with 20% overhead to $40,000 with 69% overhead, unit dose cost was set at $7.00, and cost for laboratory consumables set at $0.36 per specimen tested. Low technician and low assay costs as well as high technician and high assay costs were also calculated.

Estimation of population prevalence with pooled data. Pooling can also be used to reduce the cost of estimating population prevalence. Based on calculations from a previous study, the estimated population prevalence and 95% confidence interval (CI) were back calculated from the pooled data (6). Separate estimates were made for samples pooled by 4 and by 10. Calculations were based on the following equations: (i) Estimated prevalence: $p = 1 - [1 - (s/n)]^{1/c}$ (ii) (SD): $SD = \{[(s/n) \times (1 - s/n)]^{2-1} \quad ^{1}\}/(n \times c^2)\}^{0.5}$ (iii) 95% CI: $p \pm 1.96$ (SD) where s is the total number of presumptive-positive pools, n is the total number of pools, and c is the number of specimens in each pool.

RESULTS

Sensitivity and specificity of the pooled assays. A comparison of the distribution of S/COs for the individual and pooled samples indicated that lowering the S/CO from 1.0 to 0.20 for determining positive pools resulted in high sensitivity with a low proportion of specimens from negative pools that need to be retested individually (Fig. 1). There were two weakly positive individual specimens (i.e., an S/CO of ≥1 but <2.0) in the pilot study (pooled by 4), six weak positives in the study pooled by 4, and four low positives in the study pooled by 10. These weak positives were the only positive specimens in the pool. These pools all tested between 0.2 and 1.0 and sometimes higher.

The pooling algorithm was 100% (48 of 48) sensitive when pooling by 4 and 98.4% (61 of 62) sensitive when pooling by 10 (Table 1). Although 2.0% (2 of 99) of the negative pools of four and 7.1% (1 of 14) of the negative pools of 10 tested presumptive positive, all of the samples in these pools would be retested individually, according to the pooling algorithm. Retesting the individual samples in the presumptive-positive pools resulted in no false-positive specimens (100% specificity).

Cost analysis. For a population with 8% genital *C. trachomatis* prevalence, which is close to the 8.5% prevalence found in our study population of female U.S. Army recruits, pooling by four provided the highest cost savings. The reduction of total assay costs per specimen, which included technician time, decreased from $12.76 to $7.78, i.e., by 39%. The model demonstrated that with a 2% prevalence, pooling eight samples would reduce the cost per sample by 59%. A population prevalence graph was constructed from the model to determine the number of pooled samples that would achieve the highest cost savings (Fig. 2).

A sensitivity analysis for the cost savings model was conducted with ranges of both technician and LCR unit dose costs. For specimens tested individually, raising the base cost of the LCR unit dose from $7 to $15 resulted in an increase of the total cost per specimen tested from $12.76 to $22.87, whereas lowering the cost of the LCR unit dose to $5 reduced the total cost per specimen tested to $10.24. Similarly, raising the annual salary of the technician from $30,000 to $40,000 and assuming 28% benefits and 69% overhead increased the total cost per specimen tested from $12.76 to $13.95, whereas lowering the technician's annual salary to $20,000 and the overhead to 20% reduced the total cost per specimen tested from $12.76 to $10.89. The cost per specimen tested with the low unit dose and low technician costs was $11.43, while the high unit dose and technician costs yielded a cost of $24.06 per specimen tested.

For a population prevalence of 8% and pooling by four, ranging the unit dose cost from $5 to $15 would result in a total

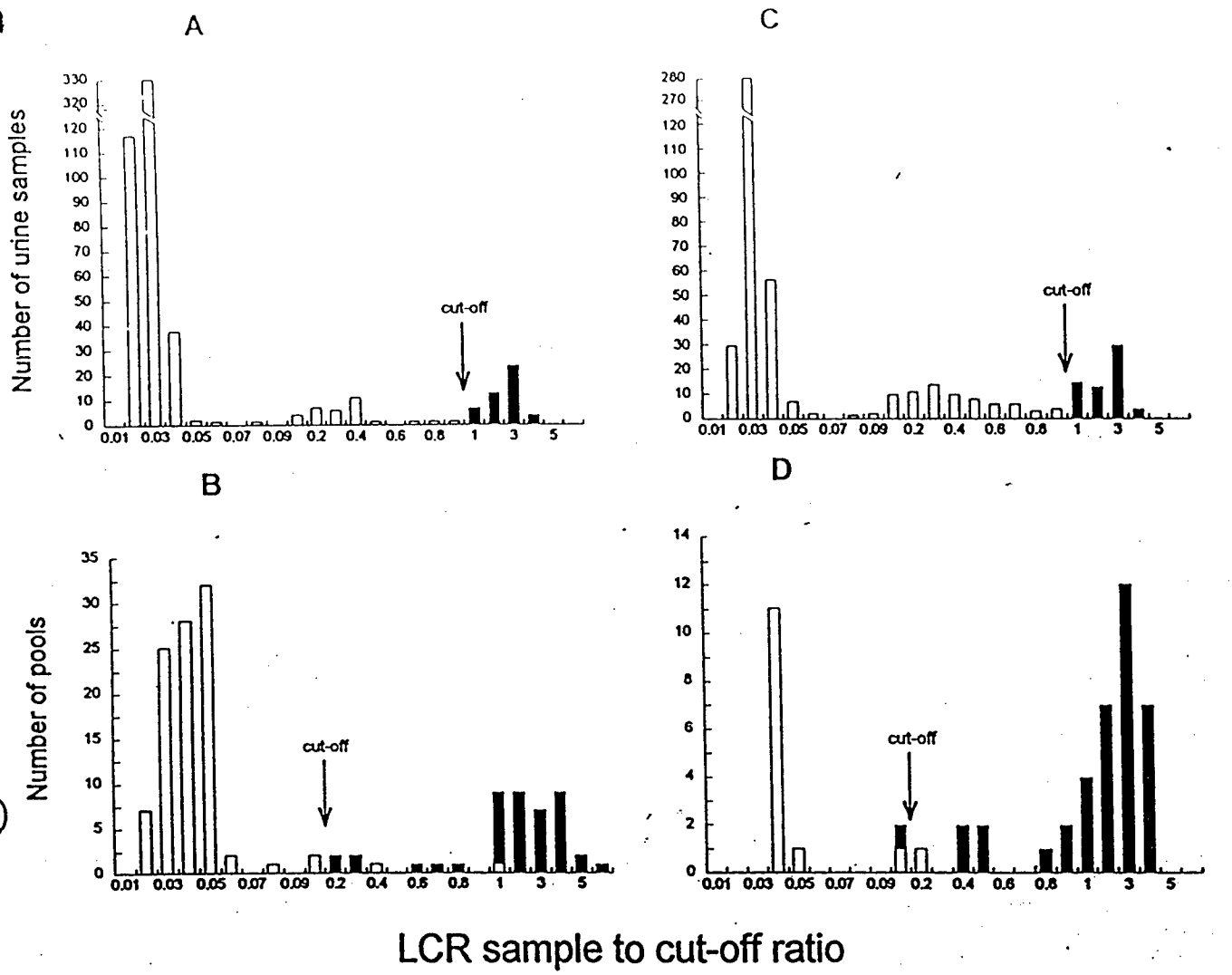

FIG. 1. Detection of genital *C. trachomatis* infection by LCR. Graphs A and C show the distribution of individual urine samples from two groups of 568 and 520 women taken from the study population. Graph B shows the distribution of the samples in A pooled by 4 (n = 142), and graph D shows the distribution of the samples in C pooled by 10 (n = 52). The S/CO for individual samples, which was 1.0, was lowered to 0.2 for pooled samples, as indicated.

cost of $6.43 and $13.17, respectively, per specimen tested. Ranging technician cost from low to high would result in a total cost increase of $6.36 and $8.68, respectively, per specimen tested. The overall savings of the pooling algorithm over individual testing ranged from 37 to 42% when low to high unit dose cost was considered. Similarly, the overall savings ranged from 42 to 38% when a low-to-high technician cost was considered. The total cost per specimen with the pooling by four algorithm with both the low unit dose and low technician cost was $5.01 per specimen tested, and that with the high unit dose and high technician cost was $14.07 per specimen tested. In all of these scenarios, pooling provided a cost savings compared with individual testing.

Estimation of population prevalence with pooled data. The observed prevalence for the individual samples in the 142 pools of 4 was 8.5% (48 of 568), and that for the 52 pools of 10 was 11.9% (62 of 520) (Table 1). The estimated population prevalence, back calculated from the number of positive pools, for the 142 pools of 4 was 9.1 (95% CI: 6.5 and 11.6), and for the 52 pools of 10 it was 12.9 (95% CI: 8.8 and 17.0). Each 95% CI included the observed prevalence of the subsample, 10.1% (110 of 1,088). Additionally, each 95% CI included values within 8 to 9%, the overall prevalence measured in a much larger sample (>10,000) of this population.

DISCUSSION

In this study we evaluated pooling of processed urine specimens for LCR detection of *C. trachomatis* for both accuracy and cost-saving ability. The high sensitivity and specificity of LCR was not affected by pooling up to 10 samples when the S/CO was adjusted from 1.0 to 0.2. Although a small percentage of negative pools tested presumptive positive, no specificity was lost with the pooling algorithm, since all specimens in pools which test presumptive positive are retested individually with the manufacturer's specified S/CO for the individual test. Since retesting negative pools does increase costs, the specificity of pools must be high.

The cost analysis model showed that depending on the prevalence of *C. trachomatis*, the number of specimens that should be pooled for optimal cost savings varies. As prevalence decreases, the pooling protocol for screening could save more than 59% of the cost per specimen compared to that for testing individual samples only. Also, early studies have shown that *C.*

TABLE 1. Accuracy of pooling urine samples for the detection of genital *C. trachomatis* infection in asymptomatic women by LCR[a]

Parameter	Result for pool size with indicated no. of samples	
	4	10
Total no. of urine samples	568	520
No. of positive specimens (%)	48 (8.6)	62 (11.9)
No. of pools	142	52
No. of presumptive-positive pools	45	39
Estimated population prevalence calculated from pooled data (95% CI)	9.1 (6.5, 11.6)	12.9 (8.8, 17.0)
No. of samples retested individually (%)	180 (31.7)	390 (75.0)
No. of positive pools (%)	43 (30.3)	38 (73.1)
Sensitivity of the pools (%)	43/43 (100)	37/38 (97.4)
Pooling algorithm sensitivity (%)	48/48 (100)	61/62 (98.4)
Specificity of the pools (%)	97/99 (98.0)	13/14 (92.9)
Pooling algorithm specificity (%)	520/520 (100)	458/458 (100)
Total no. of assays performed	322	442
No. of assays saved	246	78

[a] For the pooling algorithm, samples were first tested pooled and then presumptive-positive pools were retested individually.

trachomatis screening and treatment programs are cost effective; the Centers for Disease Control and Prevention has estimated that for every dollar spent on prevention, $12 is saved in treating sequelae (4). The use of the pooling algorithm for testing samples obtained during screening could further increase savings in health care costs.

Since *C. trachomatis* prevalence levels have ranged from 4 to 20% in various populations in the United States, pooling three to four samples is likely to provide the highest cost savings. Furthermore, the cost saved does not significantly change the sensitivity or specificity of the assay. In the event that screening is not conducted, pooling can be used to determine population prevalences over time in order to measure the benefits of disease interventions such as mass treatment or behavioral interventions. The population prevalence back calculation, described previously (6), gave an accurate estimate of the observed population prevalence in this study.

Use of the pooling algorithm would benefit investigators and program planners in two ways: (i) money saved from the use of the pooling algorithm could be applied to other areas of disease prevention and/or (ii) the amount of money allocated to screening would allow more specimens to be tested for the same total cost. Pooling samples for the detection of genital *C. trachomatis* infection in urine samples is cost saving and simple to perform and could be applicable in screening programs in the United States and in population-based research worldwide.

Pooling is a technique which could be immediately used for significant cost savings in high-volume laboratories such as state labs and referral labs. Laboratories which are currently using less sensitive and specific and less costly techniques could introduce both LCR and pooling into their laboratories.

Specific populations or laboratories that might benefit from pooling include any lab in which the combination of turnaround time and volume allows at a minimum a combination of 19 pools and retests per day. With 96 specimens at a population prevalence of about 4%, pooling by six would fill up one full run (38 test unit doses) per day. The run would include, on average, 16 pools of six and 22 retests.

Laboratory managers should consider two points before using pooling. First, processed specimens from presumptive-positive pools need to be amplified and detected individually. This additional step adds a minimum of 3 hours until individual test results for specimens in presumptive-positive pools are known. Second, laboratory managers should estimate the cost savings they expect to gain for their laboratories. This estimate is a combination of both technicians' salaries and their benefits, institutional overhead, and the prevalence of chlamydia in the populations served by the laboratory. Pooling a greater number than is recommended for certain population prevalences can cost more money than testing specimens individually.

A potential limitation of the pooling algorithm is the possibility of technician error while processed samples are pooled in the LCR run. The use of tray maps simplifies this process. Samples should be organized by skipping a space after each pooled group in the specimen rack. Thus, pooling adds no significant complexity to setting up unit doses. Additional technician error can be avoided when samples from presumptive-positive pools (detected in the previous run) are retested individually before the routine testing of the new pooled groups. Therefore, each run has a combination of samples that are retested individually and new pooled samples from the next batch of specimens.

The study laboratory has met Clinical Laboratory Improvement Act requirements for the modification of a clinical laboratory procedure from a Food and Drug Administration-approved diagnostic kit. Investigators consider performance documentation of the required study adequate for including the pooling protocol in testing clinical specimens in the study laboratory. Each laboratory that wishes to introduce pooling must meet the requirements to modify a Food and Drug Administration-approved package insert. These requirements include meeting the regulations as set forth in the Federal Register (3a).

Use of pooling processed urine samples for LCR testing of *C. trachomatis* will decrease the cost of screening, providing more evidence that screening programs can and should be implemented. Further applications of pooling include pooling urine specimens for the LCR detection of *Neisseria gonor-*

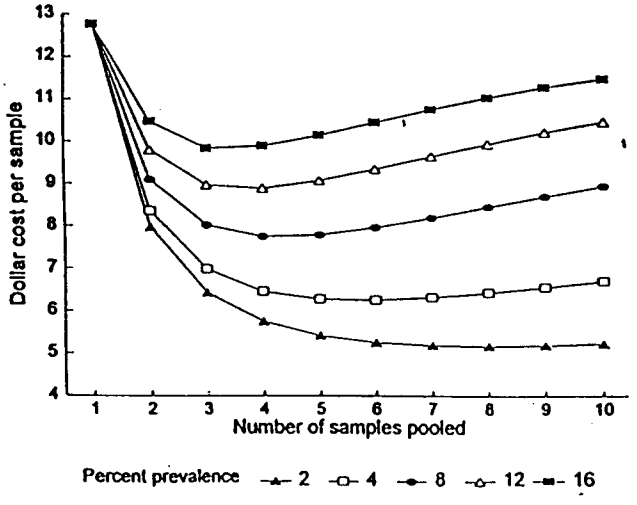

FIG. 2. Cost-saving ability of pooling processed urine specimens before the performance of the LCR test for the detection of genital *C. trachomatis* infections. The graph shows the cost per sample when the pooling algorithm was used, depending on the number of specimens pooled and taking into account various prevalences of infection in the population screened. A baseline total cost of $12.76 per individual sample which included laboratory consumables, technician time, and LCR unit dose costs was used.

rhoeae. The cost savings of pooling urine for both *N. gonorrhoeae* and *C. trachomatis* should also be considered.

ACKNOWLEDGMENTS

We acknowledge D. Perkins for her collaboration and T. and A. Kacena for their assistance.

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Control of Chlamydia trachomatis *Infections in Female Army Recruits: Cost-Effective Screening and Treatment in Training Cohorts to Prevent Pelvic Inflammatory Disease*

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Context: Chlamydia trachomatis genitourinary infections in females can lead to serious and costly sequelae. Programs such as basic (initial entry) military training with controlled points of entry offer an opportunity to screen large cohorts of women at risk for infection.

Objective: To assess the cost-effectiveness of three interventions for *C. trachomatis* infections in women beginning Army training: 1) screening using urine ligase chain reaction (LCR) by age, 2) unrestricted testing using urine LCR, and 3) universal antibiotic treatment with azithromycin.

Design: Cost-effectiveness analysis from a military perspective.

Setting and Patients: A hypothetical cohort of 10,000 women who intended to complete at least 2 years of military service was studied. Analysis was based on data from 13,204 female trainees screened for chlamydial infection at Fort Jackson, SC.

Outcomes: Program and training costs, cost of illness averted, and pelvic inflammatory disease (PID) prevented were determined for a 1-year follow-up period. Using sensitivity analysis, outcomes over 2 years were studied.

Results: At a 9.2% prevalence, no screening resulted in $220,900 in training and sequelae costs and 276 cases of PID. Screening by age produced the lowest cost $217,600, over a 1-year period and prevented 222 cases of PID for a cost-savings of $15 per case of PID prevented. Universal testing prevented an additional 11 cases of PID at a cost of $226,400, or costing $800 per additional case of PID prevented over age-targeted screening. Universal treatment prevented an additional 32 cases of PID and cost $221,100, saving $167 per additional cases of PID prevented over universal screening. Over a 2-year period, universal treatment provided the highest cost-savings and prevented the most disease.

Conclusion: Screening by age provided a cost-savings to the Army over a 1-year period. Other organizations accessing large cohorts of young women could also benefit, even in the short term, from implementation of an age-based chlamydial screening program. Universal testing or universal treatment may be warranted in which long-term societal goals, such as maximum reduction of PID, are relevant.

CHLAMYDIA TRACHOMATIS genitourinary infections and their sequelae cause significant morbidity.[1,2] These infections are often asymptomatic, especially in women, but treatment prevents the development of pelvic inflammatory disease (PID) and potentially other sequelae such as chronic pelvic pain, ectopic pregnancy, and infertility.[3] Consequently, screening of young, sexually active women has been recommended.[4,5] Recent advances in noninvasive, highly accurate diagnostic procedures have enhanced the feasibility of widespread testing of people at high risk of infection.[6,7] Screening women at risk and treating those infected can have a significant impact on the occurrence of PID, at least in the first year after treatment.[3]

Point of entry interventions using modern diagnostic procedures and single dose antibiotic treatment have been identified as potential cost-effective strategies. Temporally structured training, such as that found in the Peace Corps, the Job Training Corps, and the military, offers access to large cohorts of women for education and management of those infected. In conjunction with a study of *C. trachoma-*

The opinions presented here are those of the authors and do not necessarily represent the opinions of the U.S. Department of Defense, the Department of the Army, or the institutions with which the authors are affiliated.

The work was supported by a Women's Health Defense Initiative grant (DAMD 17-95-1-5064) from the Department of the Army.

The authors thank Dr. Rose Marie Hendrix, Ms. Dottie Ellis, Ms. Barbara Paré and Dr. Evelyn M. Barraza for their support and assistance in initiating and coordinating this study.

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Received for publication March 4, 1999, revised June 7, 1999, and accepted June 14, 1999.

TABLE 1. Parameter Estimates of Events Modeled in the Reference Case

Event	%	Cost*	Source
Chlamydia trachomatis prevalence	9.2		
LCR test of urine:			
Sensitivity/specificity	88.6/99		
Each assay		$9.15	CDC Region III contracted price†
Transportation cost/specimen		$0.22	U.S. Government shipment rate
Specimen collection and processing, and counseling, per individual		$2.89	Actual cost for employment, Fort Jackson, SC
Age ≤ 25	87.9		
Treatment clinic visit for a positive LCR:			
Administration, examination, and counseling per visit		$56.71	Actual cost, Fort Jackson, SC
Azithromycin (1-gram) effectiveness rate	96	$14.73	Public health price, DSCP‡
Cost of one clinic visit for side-effects	6.4	$56.71	Actual cost, Fort Jackson, SC
Attrition: 1 year	15		
Cost of pelvic inflammatory disease:	30		
Symptomatic	40		
2.5 gynecologic clinic visits	89	$383.00	Actual cost, Fort Jackson, SC (MEDCOM)§
5.1 inpatent days	11	$6,706.50	Actual cost, Fort Jackson, SC (MEDCOM)
Training costs lost per day		$136.00	TRADOC¶
EPTS** discharges	16.7	$6,223.00	TRADOC

* All costs are represented in 1995 U.S. dollars.
† Centers for Disease Control and Prevention, Atlanta, GA, Region III contract price.
‡ U.S. Department of Defense Supply Center, Philadelphia, PA.
§ U.S. Army Medical Command Headquarters, Fort Sam Houston, TX.
¶ U.S. Army Training and Doctrine Command Headquarters, Fort Monroe, VA.
** EPTS: Existing Prior to Service medical condition. The average cost of all discharges from the Army for a medical condition that existed before military service (EPTS) during the 8-week training period.

tis infections in women entering Army service,[7] we assessed the economic and clinical impact of three management strategies in new female recruits at the start of their military basic training: 1) targeted screening of those age 25 years or younger, 2) unrestricted testing, and 3) universal provision of antibiotic treatment.

Methods

We sought to determine the strategy that provided health improvement in terms of reduction of chlamydial infection and PID in female U.S. Army recruits for reasonable cost (i.e., to identify the cost-effective PID prevention strategy). Earlier, we observed volunteers entering the U.S. Army's largest military basic (initial entry) training post, Fort Jackson, SC.[7] In this ongoing study, we screened more than 13,000 women not seeking health care over a 2-year period and identified an overall 9.2% chlamydia prevalence using ligase chain reaction (LCR) testing of urine specimens.[7] The women originated from diverse ethnic and geographic backgrounds and were not seeking medical care. In the absence of a chlamydial control program, many probably would not have been identified as being infected or would have had a delayed diagnosis, which would have placed them at risk for developing PID. Had they developed PID during their military service, the Army would have incurred high medical costs and temporarily lost productivity during their period of illness. In addition, these women may have been at risk of discharge from the military in their first 6 months of service in accordance with the Department of Defense (DOD) policy for medical conditions existing prior to military service (EPTS). We used data from the Fort Jackson study as the basis for our model, which we developed using DATA 3.0 (TreeAge, Williamstown, MA).

From a military (i.e., a modified payer) perspective, we estimated and compared the occurrence of PID as an indicator of morbidity and costs associated with each of the three strategies at entry into the 8-week basic training program. The Fort Jackson study found young age (≤25 years) to be a feasible and reliable predictor of chlamydial infection.[7] The strategies consisted of an educational encounter in addition to: targeted screening of women age 25 years or younger using urine ligase chain reaction (LCR) (Abbott Laboratories, Abbott Park, IL), universal testing of all women using urine LCR, and universal antibiotic therapy. Costs and probabilities associated with individual events and sources for the costs are presented in Table 1. All costs are expressed in 1995 U.S. dollars. Although approximately 30,000 women enter the Army service per year, we extrapolated our total costs for this study to a hypothetical convenience cohort of 10,000 women who would enter basic training with the intention of staying in the Army for at least 2 years. Costs were measured in terms of the cost of the intervention program, the cost of training missed, and the

individual cost of PID associated with *C. trachomatis* genitourinary infection. Costs of the intervention included: the cost of a nurse or health educator to provide education and to collect, process, and ship specimens; the cost of shipping specimens; the cost of testing by a contractor-operated laboratory; the cost of follow-up, including a clinic visit for women who test positive; the cost of single-dose azithromycin (1 gram) for treatment; and the cost of a clinic visit for complaints of possible side-effects associated with antibiotic treatment.

The outcomes evaluated for each strategy included PID prevented and overall costs expended. Measurement of prevented symptomatic and asymptomatic PID were included as clinical outcomes. However, there were no financial benefits associated with asymptomatic PID because of the 1-year analytic horizon used in the reference case. The cases of prevented PID estimated in this analysis were assumed to be attributable to one of the screening strategies because women not seeking health care were used in the analysis.

Cost of illness data represent military costs per outpatient visit and inpatient bed day, including 2.5 gynecologic or obstetric outpatient visits for PID and 5.1 inpatient regular care bed days for PID, as determined from Army records for 1996 (U.S. Army Medical Command Headquarters [MEDCOM], Fort Sam Houston, TX). Costs for medical care in the Army vary considerably. Costs at Fort Jackson are considered average within the military system and were used for all health care costs, even though the soldiers in the model could receive medical care in many other locations after leaving Fort Jackson (MEDCOM, Fort Sam Houston, TX).

Lost training costs represent costs lost on female recruits who were discharged because of PID after basic training had already been initiated, including direct (supplies and salaries associated with instruction) and indirect (site and service support, housing) costs. In addition, the training costs lost while a woman receives treatment for PID were included. A considerable part of the first year in the military is spent in training. Advanced training after basic training is varied, including programs such as training for becoming a chaplain's assistant or an aviation mechanic. These later training costs vary considerably. After completion of training, lost costs for military nonproductive time depend on many variables, including rank. Because of the complexity of this situation, we assumed that each day a soldier was unproductive in training or work would result in an average loss of $136 (U.S. Training and Doctrine Command Headquarters [TRADOC], Fort Monroe, VA). Projected attrition rates were obtained from a U.S. Army personnel model.[8]

Ligase chain reaction screening of urine for *C. trachomatis* in asymptomatic military females undergoing a PAP test had an 88.6% sensitivity and a specificity of 99.0% compared to a gold standard including cervical culture and adjudicated LCR-positive culture negative results.[9] In our study, overall, 87.9% of the women studied were age 25 or younger and this group contained 95.3% of the positives.[7] Other events (probabilities) in our model included the following: 100% of women with an LCR positive chlamydia urine test and those in the universal treatment group would be administered a single dose (1 gram) of azithromycin, assumed to be 96% effective;[10,11] an estimated 6.4% of treated women would experience moderate to severe side-effects[10] and require a clinic visit; and an estimated 13% of all women who begin basic training would drop-out of training for reasons unrelated to chlamydia infection, with attrition averaging 2% for their first year in the Army after basic training for a total attrition of 15% in the first year.[8] Sequelae probabilities for the model were obtained from the medical literature or Fort Jackson records. We considered only women with chlamydial infections at the time of entry into military basic training and did not consider reinfections. Of those women who remained in the military, 30% with uncured chlamydial infections would develop PID, 40% of whom would develop symptoms.[12–15] Consistent with the experience at Fort Jackson, an estimated 11% of women with symptomatic PID would require inpatient treatment; and 89% would require only outpatient treatment. An estimated 16.7% would be discharged from the military because of development of symptomatic PID within their first 6 months of service. Asymptomatic PID is associated with no costs of illness during the first year.

The results of our model are expressed for a 1-year analytic horizon for a population of 10,000 women with a *C. trachomatis* prevalence of 9.2% when beginning basic training as determined by urine LCR. All costs are expressed in 1995 U.S. dollars and future costs are discounted at an annual rate of 3%. All parameters were varied in univariate sensitivity analyses to determine the effect of changing parameter values on the results. In the absence of data regarding sexual mixing patterns, the time of infection before basic training, screening programs after basic training, and reinfection, it is difficult to assess the time frame after the 1-year horizon during which the benefits from the one-time strategy during basic training will be experienced. Because of these unknowns, we focused in the reference case on the morbidity benefits and prevented costs of illness associated with PID occurring within the first year after screening. However, the development of chronic pelvic pain (CPP) in women with PID within the first 2 years after infection is common.[16] Consequently, in a multivariate sensitivity analysis, we also extended the analytic horizon in which benefits would be realized from 1 to 2 years. This analysis considered that 18% of the women with PID (symptomatic and asymptomatic) would develop CPP16 and would require an inpatient visit of similar duration to that of PID (i.e., 5.1 days); an attrition rate of 14% was considered for the second year and a half-year attrition rate of 7% was estimated.[8] The cost of chronic pelvic pain was

TABLE 2. Cost-Effectiveness of Three *C. trachomatis* Infection Control Strategies: A 1-Year Analytic Horizon, Applied to 10,000 Women Starting Army Basic Training with a Prevalence of 9.2%*

Management Strategy	Program Costs 1995 U.S.$	Total Cost (Program + Sequelae Costs)	Incremental Cost Differential Over Next Least Expensive Strategy	Expected Cases of PID*	Cases of PID* Prevented Over Next Most Effective Strategy†	Incremental Cost-Effectiveness Ratio§
No screening	—	$220,900	—	276	—	Noprevention
Targeted screening	$174,400	$217,600	−$3,300	54	222	$15
Universal testing	$192,000	$226,400	$8,800	43	11	$800
Universal treatment	$212,600	$221,100	−$5,300	11	32	$166

* Age-based targeted screening provides the highest cost-savings.
† Outcome is limited to cases of symptomatic and asymptomatic pelvic inflammatory disease (PID).
‡ Effective = Effective in preventing PID.
§ Incremental cost-effectiveness ratio:

$$\frac{\text{Total Cost of Strategy A} - \text{Total Cost of Strategy B}}{\text{Cases of PID Occurring with Strategy A} - \text{Cases of PID Occurring with Strategy B}}$$

where, Strategy A is the strategy under question and Strategy B is the next most effective strategy for preventing PID.

modeled as the inpatient cost of 5.1 inpatient days, discounted at a rate of 3% for 2 years.

Results for each strategy are reported in terms of 1) cases of PID prevented (strategy$_x$ compared to no screening option), 2) incremental cases of PID prevented (strategy$_x$ compared to next most effective strategy$_y$), 3) program costs, 4) sequelae costs, 5) total costs (program costs + sequelae costs), 6) total average cost-savings (total cost of strategy$_x$ compared to cost of no screening option), 7) total incremental cost-savings (total cost of strategy$_x$ compared to next most effective strategy$_y$), and 8) the incremental cost-effectiveness ratio (cost of one strategy$_x$ compared to the cost of the next most effective strategy$_y$ relative to the additional number of cases of PID prevented by strategy$_x$ over strategy$_y$).

Results

Cost-Effectiveness Analysis

In the absence of screening in the cohort of 10,000 women, an expected 276 women would develop asymptomatic or symptomatic PID from the total of 920 cases of *C. trachomatis* infections in 1 year at a total cost of illness and lost training of $220,900 (Table 2). Targeted screening of women age 25 or younger would result in effective treatment of 740 *C. trachomatis* infections, preventing an estimated 222 cases of asymptomatic and symptomatic PID. Targeted screening by age would cost $217,600 (all costs to include: program costs, cost of illness, and cost of training lost), saving $3,300 over no screening and representing the most cost-saving strategy. Targeted screening saved $15 for each additional case of PID prevented.

Universal testing of all women would result in effective treatment of 777 *C. trachomatis* infections, preventing an additional 11 cases of PID over targeted screening. Universal testing would have a total cost of $226,400, representing a cost of $5,500 over no screening and a cost of $800 per additional case of PID prevented over targeted screening.

Universal treatment would result in effective treatment of 883 *C. trachomatis* infections and prevent an additional 43 cases over targeted screening and 32 cases of PID over universal testing. Universal treatment would have a total cost of $221,100, representing an increase of $200 over no screening, a cost of $81 per additional case of PID prevented over targeted screening, and a savings of $166 per additional case of PID prevented over universal testing.

Sensitivity Analysis

To address concerns regarding variations in the parameter estimates used in the model, we performed sensitivity analyses, which varied the probability and cost estimates of events over plausible ranges and explored the effect of an expanded analytic horizon. The model was sensitive to changes in several estimates.

Univariate Sensitivity Analysis

If antibiotic costs per individual increased from $14.73 to $18.45 per individual, or greater than 13% of all women treated experienced side-effects necessitating a clinic visit, targeted screening no longer saved cost compared to no screening. However, if antibiotic costs per individual decreased to $14.35 or if fewer than 6% of all women treated experienced side-effects that required a clinic visit, universal treatment provided a cost-savings over all strategies considered. If the chlamydial prevalence dropped to <9%, the program costs for any of the three strategies compared in this model would exceed the savings provided by prevented

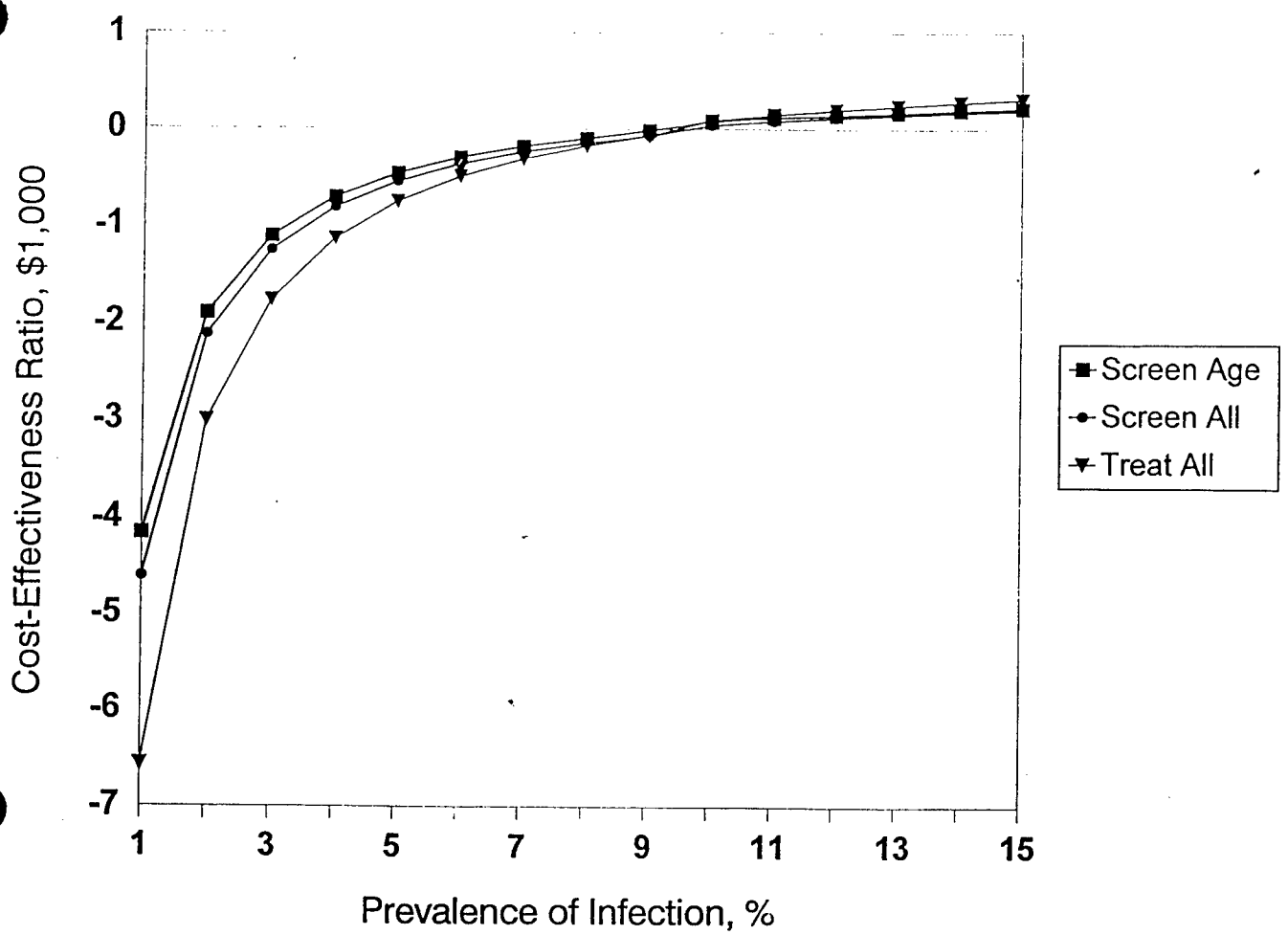

Fig. 1. Univariate sensitivity analysis: cost per case of pelvic inflammatory disease (PID) prevented as chlamydia prevalence varies over a 1-year horizon. Average cost-effectiveness ratio =

$$\frac{\text{Total Cost of Strategy} - \text{Total Cost of No Screening}}{\text{Cases of PID Occurring with Strategy} - \text{Cases of PID Occurring with No Screening}}$$

The x-axis intercept of the dashed line represents a chlamydia prevalence of 9%, at which point age-based screening provides a cost-savings over no screening.

medical costs and prevented lost training costs. However, if the chlamydia prevalence increased only marginally to >9.5%, universal treatment provided a higher cost-savings than targeted screening. If the prevalence was at least 9.7%, all strategies provided a cost-savings over no screening (Fig. 1). If assay costs increased more than $12.64, targeted screening did not provide a cost-savings over no screening. However, if assay costs decreased to $4.88 or less, universal testing provided a cost-savings over all of the strategies analyzed here.

Multivariate Sensitivity Analysis

Under a 2-year analytic horizon considering prevented chronic pelvic pain, universal treatment became the most cost-saving strategy (Table 3). Universal testing saved $300 over targeted screening. Universal treatment saved $32,400 over targeted screening. Furthermore, in a sensitivity analysis considering prevented CPP and PID over a 2-year period, even at a chlamydia prevalence as low as 3.4% (Fig. 2), targeted screening provided cost-savings over no screening. Universal treatment provided the highest cost-savings relative to other interventions at prevalences >7% (Fig. 2).

Discussion

C. trachomatis infections represent a significant source of morbidity and health care expenditures.[17] Considering the impact of one time screening and treatment on PID prevention over a 1-year period, targeted screening by age provided the highest cost-savings. This is consistent with other cost-effectiveness analyses designed to evaluate chlamydia

TABLE 3. Cost-Effectiveness of Three *C. trachomatis* Infection Control Strategies: A 2-Year Analytic Horizon, Applied to 10,000 Women Starting Army Basic Training with a Prevalence of 9.2%*

Management Strategy	Total Cost (Program + Sequelae Costs)	Incremental Cost Differential Over Next Least Expensive Strategy	Expected Cases of PID†/CPP‡	Cases of PID†/CPP‡ Prevented Over Next Most Effective Strategy§	Incremental Cost-Effectiveness Ratio¶
No screen	$452,900	—	276/36	—	No prevention
Targeted screening	$262,800	−$190,100	54/7	222/29	$856
Universal testing	$262,500	−$300	43/6	11/1	$27
Universal treatment	$230,400	−$32,100	11/1	32/5	$1,003

* Universal treatment is the most cost-effective strategy.
† PID = cases of symptomatic and asymptomatic pelvic inflammatory disease.
‡ CPP = chronic pelvic pain.
§ Effective = Effective in preventing PID.
¶ Incremental cost-effectiveness ratio:

$$\frac{\text{Total Cost of Strategy A} - \text{Total Cost of Strategy B}}{\text{Cases of PID Occurring with Strategy A} - \text{Cases of PID Occurring with Strategy B}}$$

where, Strategy A is the strategy under question and Strategy B is the next most effective strategy for preventing PID.

prevention and control strategies.[13,15] However, universal treatment prevented the greatest amount of PID for only a marginal increase in cost per case of PID prevented over age-targeted screening. The long-term impact of the sexually transmitted diseases (STD) educational experience provided with each of the interventions and the impact of treating a *C. trachomatis* infection regardless of later reinfections, is unknown. However, the possibility exists for positive effects extending beyond 1 or 2 years.

In this study we considered that LCR testing of urine would be conducted under contract, as a most conservative cost approach. If the U.S. military were to initiate testing on a large scale at many or all training centers, a significant reduction in the cost of the LCR assay may occur. In addition, we considered that specimen collection, processing and shipment, and counseling for STDs at the time of specimen collection would require a new dedicated contract employee. Integrating testing with other routine recruit screening procedures or combining the personnel functions of a chlamydia control program with another program, such as HIV screening, may reduce personnel costs.

Diagnostic tests that can be used with urine specimens eliminate the need for a pelvic examination to collect a cervical specimen. This technology increases the number of women who can be screened per unit of time and improves the cost-effectiveness of a chlamydial screening program.[18] Administrative management of large numbers of people at the point of entry to large training programs, such as military basic training, is stressful because of the many activities that must be accomplished in a short period of time. Addition of a medical screening component to this process will require additional time. However, these negative aspects must be viewed in light of the benefits provided.

The U.S. military has successfully used universal antibiotic prophylaxis to control respiratory infections.[19] However, concerns have been raised regarding emerging resistance to antibiotics that may be associated with mass therapy, and these issues must be addressed. In addition, the proportion of treated young women who would seek health care for side-effects associated with therapy requires documentation. Until the needed studies are conducted, universal administration of antibiotics for chlamydial infections and their sequelae may be discouraged, even in the presence of a high prevalence of disease.

The full benefit of a chlamydial screening program on women entering the Army requires greater definition. When data on chronic pelvic pain, infertility, and ectopic pregnancy become available and a long-term societal perspective is taken, universal testing or universal treatment may be preferred over targeted screening. Benefits derived from *C. trachomatis* prevention and control programs for men must also be addressed, as well as periodic evaluations for reinfection in males and females. It is likely that education, screening, and treatment of men and women would decrease the potential for reinfection and costly sequelae for both sexes. A study of *C. trachomatis* infections in males beginning Army basic training is in progress.

The reference case analysis intentionally modeled a narrow set of potential benefits. This conservative approach was undertaken for two reasons: 1) to demonstrate the immediate or short-term benefits associated with chlamydial screening, and 2) to limit the effect of unknown variables, such as reinfection, sex partner change, and repeated screening efforts on the estimated benefits of one time screening. As expected, the health benefits to be considered in our model greatly impacted the outcome of the analysis. Ex-

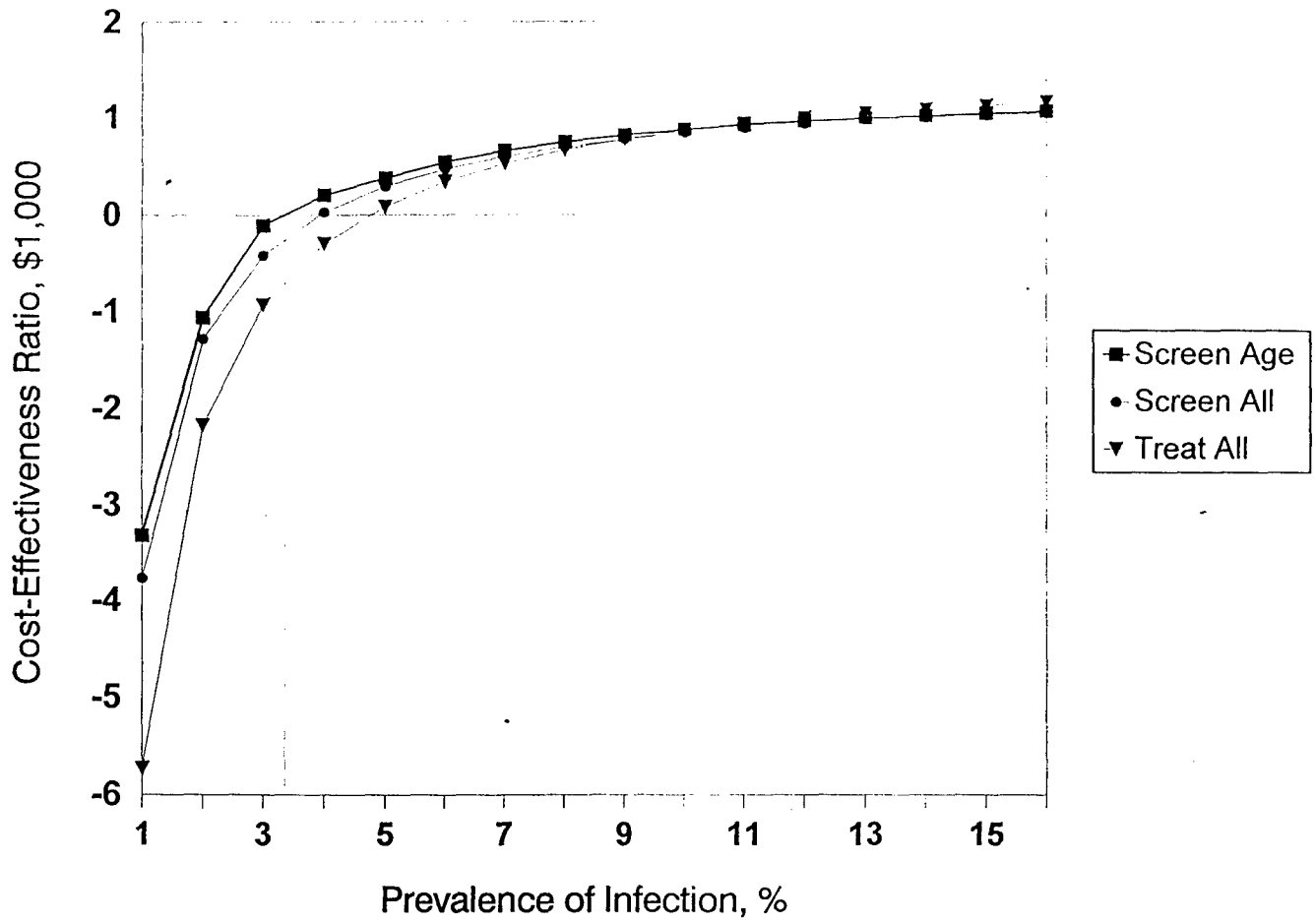

Fig. 2. Multivariate sensitivity analysis: cost per case of pelvic inflammatory disease (PID) prevented as chlamydia prevalence varies over a 2-year horizon (including the cost of a case of chronic pelvic pain prevented). Average cost-effectiveness ratio =

$$\frac{\text{Total Cost of Strategy} - \text{Total Cost of No Screening}}{\text{Cases of PID Occurring with Strategy} - \text{Cases of PID Occurring with No Screening}}$$

The x-axis intercept of the dashed line represents the chlamydia prevalence of 3.4%, at which point age-based screening provides a cost-savings over no screening.

tending the analysis toward a societal perspective by including the prevention of chronic pelvic pain and PID rapidly affects the cost-saving ability of each strategy. In a 2-year analytic horizon, universal treatment provided the highest cost-savings and prevented the most disease. Furthermore, much of the morbidity associated with infection will occur after several years. Extension of the analytic horizon beyond 2 years and inclusion of outcomes such as ectopic pregnancy and infertility would drive the cost of illness higher and would increase the cost-effectiveness of all three strategies because of the gains in prevented medical care costs for society as a whole. Such long-term benefits deserve consideration by the military and civilian public health authorities because the costs and morbidity will not be borne exclusively by the military.

From a limited 1-year perspective in our analysis, targeted screening should be considered a conservative management strategy. However, universal testing and universal treatment may be warranted in settings where long-term goals, such as preventing infertility, are desired. On average, the Army will probably provide initial entry training for approximately 30,000 women each year. Up to half may not become full-time military members. These women are members of the National Guard and the reserve components and will return to civilian life after completing their 8-week military training programs. For many of these women, the benefits of a military chlamydial control program will be realized after they return to their civilian community. STDs are a joint military-civilian problem.[20] High-risk young people are continually moving between the military and civilian sectors as they enter and exit military service, and many military installations exist in close proximity to towns and cities. It is thus inappropriate to consider STDs in military recruits and service members an exclusively mili-

tary problem. Society, in general, should expect to receive short- and long-term benefits from education and other interventions conducted during military service. Combined military and civilian resourcing to provide screening and treatment to young people at high risk who pass through such a controlled portal of entry should be considered as a key public health opportunity not only for the military but for society as a whole.

Considering the high prevalence of *C. trachomatis* genital infection in young sexually active U.S. women, development of a management strategy for all training programs where tens of thousands of women annually pass through a defined and controlled point of entry (e.g., Army recruit training) should be a high priority. This initiative could be considered part of the national strategy for control of STDs and their sequelae. These training programs with well-defined entry cohorts provide a unique opportunity to educate, diagnose, and treat for the benefit of society in general.

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CHLAMYDIA TRACHOMATIS INFECTIONS IN FEMALE MILITARY RECRUITS DIAGNOSED BY URINE-LCR: PREVALENCE AND RISK FACTORS

C.A. Gaydos[1], G. Jaschek[1], M.R. Howell[1], B. Pare[1], K. Clark[1], D. Ellis[2], K. McKee[3], R. Hendrix[2], J. Gaydos[4], T.C. Quinn[1,5]

[1]Johns Hopkins Univ., Baltimore, MD; [2]Ft. Jackson, SC; [3]Ft. Bragg, NC; [4]Ctr. for Health Promotion and Prev. Med., Aberdeen Proving Ground, MD; [5]NIAID, NIH, Bethesda, MD.

OBJECTIVES: This study was undertaken to determine the prevalence of chlamydial infections in new female military recruits and to predict which risk factors are useful for future screening.

METHODS: Incoming female recruits undergoing medical inprocessing at Ft. Jackson, SC, were voluntarily recruited into the study and asked to provide a urine sample and answer a short questionnaire. Urines were processed and tested by ligase chain reaction (LCR) [Abbott Labs, Abbott Park, IL] for chlamydial DNA. Prevalence, demographics, and risk factor information were analyzed by univariate and multivariate logistic regression models (Stata Corp., College Station, TX).

RESULTS: From 3,283 females available, 1,965 (59.9%) volunteered from January 21 through April 7, 1996. There were evaluable data from 1954 females. Demographic characteristics of this population included: 83.9% were age 25 or younger, 49.6% were Caucasian, 36.2% African American, and 14.2% were other races. The prevalence for *C. trachomatis* by urine LCR for the population was 6.7% (130 of 1954). By questionnaire, 94.2% reported having had vaginal sex, 22.8% had more than 1 sex partner in the previous 90 days, 23.9% had a new sex partner in the previous 90 days, and only 17.4% always used condoms. A prior history of chlamydial infections was reported in 9.7%, gonorrhoeae in 3.4%, syphilis in 0.41%, and trichomonas infection in 5.7%. By age categories, prevalences were 7.4% (age 17-20); 7.3% (21-25); 3.5% (26-30); and 1.2% (31-35). For further analyses, the 2 youngest age categories were combined into a variable called "young" (age 17-25; prevalence = 7.4%). By race, prevalences were 4.2% for Caucasian, 10.0% for African American, and 6.5% for other races. Univariate analysis identified 4 significant risk factors. Condom use and prior diagnosis of chlamydia, gonorrhoeae, syphilis, or trichomonas were not significant ($p < .05$). By multivariate logistic regression the most useful risk factors were young age, African American, and having a new sex partner.

Univariate Analysis

Risk Factor	O.R.	95% C.I.
Young (17-25 yr)	2.71	1.36-5.39
African American	2.53	1.70-3.76
>1 Sex Partner	1.64	1.12-2.41
New Sex Partner	1.77	1.21-2.57

Multivariate Logistic Regression Analysis

Risk Factor	O.R.	95% C.I.
Young (17-25 yr.)	2.49	1.24-4.99
African American	2.68	1.78-4.00
New Sex Partner	1.85	1.26-2.71

CONCLUSIONS: Urine-based screening for C. trachomatis was effective in a female military recruit population. Acceptability was high, specimens were readily obtained, and the assays were easy to perform. The results demonstrated a high prevalence (6.7%) for young females from a geographically and demographically diverse population, indicating the need for an active chlamydial control program.. Screening all young female recruits age 25 or less in this population would mean that 83.9% would be screened and 93.1% of all the positives would be diagnosed. A targeted chlamydial screening program, such as urine-LCR testing, has the potential to prevent many cases of pelvic inflammatory disease and ectopic pregnancy in military women.

Third Meeting of the European Society for Chlamydia Research; Vienna, Austria. Sept. 11-14, 1996.

CHLAMYDIA TRACHOMATIS INFECTIONS IN FEMALE SOLDIERS AT FT. JACKSON AND FT. BRAGG DIAGNOSED BY URINE-LCR

C.A. Gaydos[1], K. Clark[2], G. Jaschek[1], M.R. Howell[1], B. Pare[1], D. Ellis[1], K. McKee[4], R. Hendrix[3], T.C. Quinn[1,4], J. Gaydos[5]. [1]Johns Hopkins Univ., Balt., MD; [2]Walter Reed Army Institute of Research, Wash., DC; [3]Ft. Jackson, SC; [4]Ft. Bragg, NC; [4]NIAID, NIH, Bethesda, MD; [5]Ctr. for Health Prom. and Prev. Med., Aberdeen P.G., MD.

REVISED ABSTRACT

This study determined the prevalence of chlamydial infections in military females and predicted useful risk factors for future screening programs. Three populations were studied. Female recruits (RECRUITS) undergoing inprocessing and symptomatic women at the Troop Medical Clinic (TMC PATIENTS) at Ft. Jackson, as well as females having a PAP test performed (PAP PATIENTS) at Ft. Bragg, were voluntarily recruited into the study. Each was asked to provide a urine sample and answer a questionnaire. Urines were tested by ligase chain reaction (LCR) [Abbott Labs, Abbott Park, IL] for chlamydial DNA. Prevalence, demographics, and risk factors were analyzed by univariate and multivariate logistic regression models (Stata Corp., College Station, TX). RECRUITS: From 4,815 recruits available, 3,189 (66.2%) volunteered from January 21 to June 23, 1996. Evaluable data from 3,177 recruits showed: 86.1% were age 25 or younger, 52.9% were Caucasian, 34.5% were African American, and 12.6% were other races. The prevalence for *C. trachomatis* by urine LCR for the population was 7.3% (232 of 3,177). By questionnaire, 93.5% reported having had vaginal sex, 23.3% had more than 1 sex partner in the previous 90 days, 25.4% had a new sex partner in the previous 90 days, and 17.2% always used condoms. A prior history of chlamydial infections was reported in 9.4%, gonorrhoeae in 3.2%, syphilis in 0.6%, and trichomonas infection in 4.9%. By age, prevalences were: 8.5% (age 17-20); 7.4% (21-25); 3.2% (26-30); and 1.6% (31-35). For further analyses, the 2 youngest age categories were combined. By race, prevalences were 4.3% for Caucasian, 11.4% for African American, and 8.5% for others. Univariate analysis identified 4 significant risk factors: young age (17-25 years), African American, > 1 sex partner, and new sex partner. Condom use and prior diagnosis of chlamydia, gonorrhoeae, syphilis, or trichomonas were not significant. By the multivariate model, the most useful risk factors were young age (OR 3.04), African American (OR 3.06), and having a new sex partner (OR 1.68). TMC PATIENTS: Volunteers included 296 symptomatic soldiers. Prevalences were: 12.8% overall; 13.4% for $\leq$ 25 yr.; 5.5% for Caucasian; and 18.1% for African American. PAP PATIENTS: Among 171 volunteers, prevalences were: 8.0% overall; 10.1% for $\leq$ 25 yr.; and 10.0% for African American. SUMMARY. Urine-based screening for C. trachomatis was effective in a female military population. Acceptability was high, specimens were readily obtained, and assays were easy to perform. A high prevalence (7.3%) for young recruits from a demographically diverse population indicates the need for an active chlamydial control program. Screening young female recruits age 25 or less would mean that 86.1% would be screened and 94.8% of positives would be diagnosed. A targeted chlamydial screening program has the potential to prevent many cases of PID and ectopic pregnancy.

Presented at U. S. Army Preventive Medicine Conference; Charlotte, N.C. September 16-20, 1996.

Use of Urine Ligase Chain Reaction (LCR) to diagnose C. trachomatis in female soldiers at Ft. Jackson and Ft. Bragg.

C.A.Gaydos, D.Pham, M.R.Howell, B.Pare, D.Ellis, K.Clark, K.McKee, R.Hendrix, J.Gaydos, T.C. Quinn, Johns Hopkins Univ, Balt. MD. Ft. Jackson, SC, Ft Bragg, NC, CHPPM, Aberdeen, MD, NIH, NIAD, Bethesda, MD.

This ongoing study used urine LCR to determine the prevalence of and risk factors for chlamydial infections among military females. Three different populations were screened: recruits who were beginning military service, symptomatic patients attending a Troop Medical Clinic (TMC), and asymptomatic women having a PAP test. Each soldier provided a urine and answered a questionnaire. Urines were tested by LCR (Abbott Labs) and the PAP patients were also tested by cervical culture. In 5,096 women screened, the prevalence was 8.6%. The recruits, TMC, and PAP populations had prevalences of 8.2%, 12.1%, and 7.1%, respectively. The mean age was 22; 50.5% were Caucasian; 23.9% had more than 1 sex partner in the last 90 days; and 26.3% had a new sex partner. Only 17.1% used condoms consistently; 9.7% had a chlamydial infection previously. Univariate analysis identified several risk factors useful for predicting chlamydial positivity: young age, African-American race, more than 1 sex partner, and a new partner. Urine-based screening was effective in screening large numbers of women and was highly acceptable. Compared to culture, the sensitivity of LCRwas 88.2% in the asymptomatic group. A universal or targeted screening program is being developed and should prevent acute chlamydial morbidity and sequelae such as PID.

Presented at the American Society of Microbiology; Miami, Florida; 5/97.
Abstract #C-377

3RD ANNUAL

Uniformed Services

RECRUIT & TRAINEE HEALTH CARE

Symposium

AGENDA

"Reducing Attrition, Promoting Health"

STERNBERG AUDITORIUM
(WRAIR BUILDING)

Walter Reed Army
Institute of Research
Washington, DC

May 19-21
1997

1615-1630 **Cost Effectiveness Analysis of PAP Smear Screening at Basic Training**
CAPT Ken Long MC, USN
Senior Medical Officer, Branch Medical Clinic
Parris Island, South Carolina

1630-1700 **Exercise Related Mortality in Recruit Basic Training**
COL John W. Gardner MC, USA Professor of Epidemiology
USUHS, Bethesda, Maryland

1800 Buses depart to the Navy Officers' Club for dinner

1830-2000 Dinner at Navy Officers' Club

Special Awards for the Developers of the Adenovirus Vaccines:

Dr. Robert M. Chanock
Dr. Harold S. Ginsberg
Dr. Robert Couch
MG (Ret.) Philip K. Russell MC, USA
COL (Ret.) Franklin H. Top MC, USA
COL (Ret.) Edward L. Buescher Jr., MC, USA

Presentation of Awards by:
COL Joel C. Gaydos MC, USA

Reducing Attrition, Promoting Health: An Historian's View"
Special Guest Speaker:
Dr. Dale C. Smith, USUHS

Tuesday, May 20

0730-0800 Continental Breakfast (WRAIR)

INFECTIOUS DISEASE SECTION

0800-0840 **"Chlamydia Screening in Recruits"**
Charlotte Gaydos, Assistant Professor,
Infectious Disease Division, School of Medicine,

0840-0905 **"Sexual Risk Behaviors of Recruits at Fort Jackson, S.C."**
LTC (P) Joan Eitzen ANC, USA
USACHPPM, Aberdeen Proving Ground, MD

0905-0930 **"Serum Titer Directed Immunization"**
LCDR Margaret A.K. Ryan MC, USA
Head, Division of Preventive Medicine
Naval Hospital, Great Lakes, Illinois

0930-0945 BREAK (exhibit area outside Sternberg Auditorium)

0945-1015 **Booster Phenomenon Associated with Sequential Tuberculin Skin Testing in Marine Recruits**
CDR Edward Gastaldo MC, USN
Medical Epidemiologist, Beaufort, SC

1015-1045 **"Respiratory Disease Control in Military Basic Training Camps"**
CAPT (sel.) Greg Gray, MC, USN
Naval Health Research Center, San Diego, CA

1045-1055 **"National Military Invasive *Streptococcus pyogenes* Surveillance"**
Mr. Tony Hawksworth, Naval Health Research Center
San Diego, CA

1055-1105 **"National Military Advenovirus Surveillance"**
Dr. Pulak Goswami, Naval Health Research Center
San Diego, CA

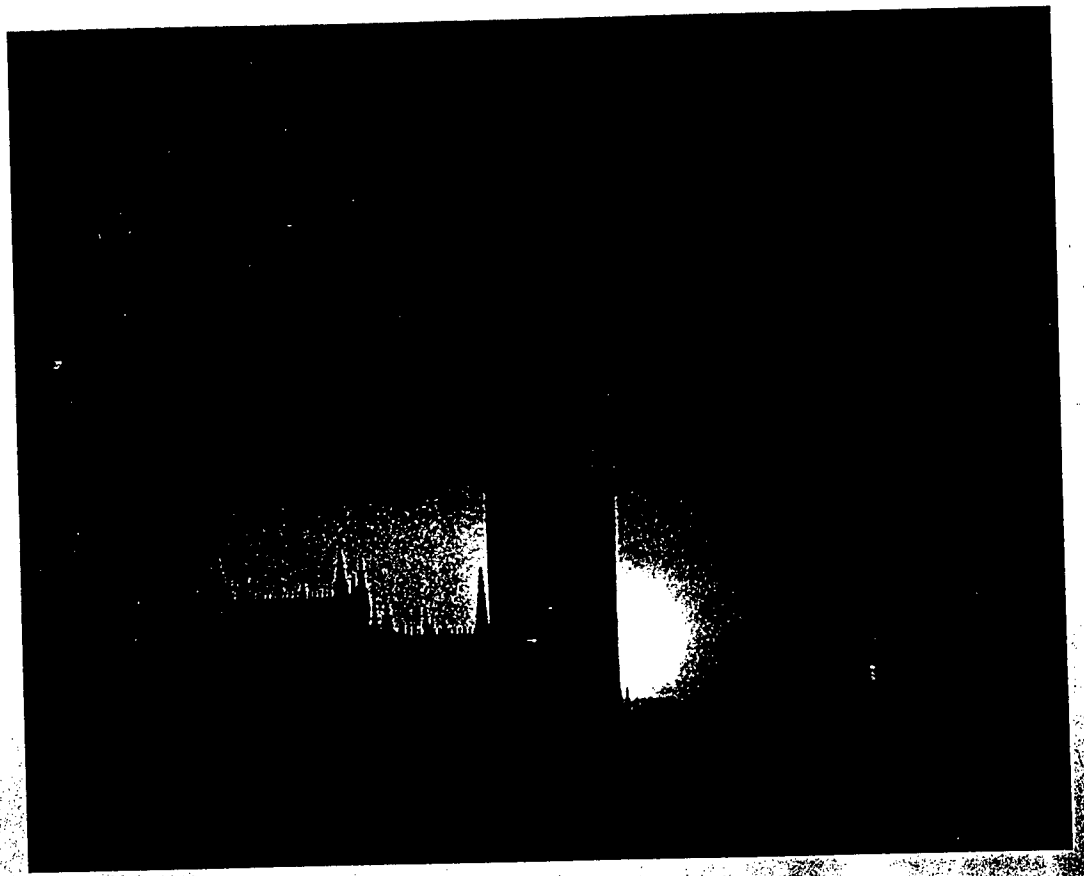
1105-1140 **"Advenovirus: A Past and Present Treat"**
COL Joel C. Gaydos, MS, USA
Director, Clinical Preventive Medicine
USACHPPM, Aberdeen Proving Ground, MD

1140-1200 **Infectious Disease Panel Discussion**
(Above Speakers)
Moderator: CAPT Jon D. Bayer MC, USN

1200-1315 Lunch (box lunches/poster session #1/3rd Floor, WRAIR)

INTERNATIONAL CONGRESS OF SEXUALLY TRANSMITTED DISEASES

Appendix 11.2



PROGRAM AND ABSTRACTS

The 12th Meeting of the International Society of Sexually Transmitted Diseases Research (ISSTDR) held jointly with the 14th Regional Meeting of the International Union Against Sexually Transmitted Infections (IUSTI)

SEVILLE, SPAIN

19 - 22 October 1997

respectively). The above results are clinically significant, when considering the low prevalence of *C. trachomatis* IgG & IgA antibodies observed in the three control groups; blood donors (8%, 4.4%), children (3%, 0%) and pregnant women (6%, 0%), respectively.

The high specificity and sensitivity of SeroCT for the specific detection of *C. trachomatis* antibodies makes this new generation test, an accurate efficient and cost effective screening tool for the differential diagnosis between *C. trachomatis* and *C. pneumoniae* infections.

P511 CHLAMYDIA TRACHOMATIS INFECTIONS IN SYMPTOMATIC AND ASYMPTOMATIC COUPLES

Petersen EE, Clad A., Univ. Frauenklinik Freiburg, D-79106 Freiburg, Germany

Objective: Normally, only symptomatic patients are tested for chlamydial infections. Little is known about partner infection in asymptomatic couples. First void urines of symptomatic (STD outpatient clinic) and asymptomatic females and their asymptomatic partners (genital chlamydial prevalence study with LCR on 4.381 persons, Germany) were collected to assess the prevalence of Chlamydia trachomatis in couples.

Methods: Urines and cervical swabs were tested with the ligase chain reaction (LCR, Abbott). In the prevalence study only one urine from each woman and her male partner was collected. In symptomatic women cervical swabs and urine and partner urines were tested and retested at follow-up visits.

Results: Only couples with one or both partners positive in the chlamydial LCR are presented here. Of 53 *symptomatic* women 37 (69%) were positive. 39 (72%) of the asymptomatic male partners had positive urines. In 21 (38%) couples both partners were positive. In 84 *asymptomatic* couples 46 (55%) of the women and 67 (80%) of their male partners were positive. In 29 (36%) couples both partners were positive.

Conclusion: In symptomatic as well as in asymptomatic women significantly more chlamydial infections could be detected when also testing their male partners. Testing of one male (urine) and one female sample (urine or cervical swab) by LCR appears to be more cost-efficient than testing several female samples.

P513 COST-EFFECTIVENESS OF SCREENING vs MASS THERAPY FOR *C. TRACHOMATIS* IN FEMALE ARMY RECRUITS

Howell MR[1], McKee K[2], Ellis D[3], Gaydos J[3], Hendrix R[2], Quinn TC[4,5], Gaydos CA[1]
[1]*The Johns Hopkins University, Baltimore, MD;* [2]*Fort Bragg, NC;* [3]*Fort Jackson, SC;* [4]*CHPPM, Aberdeen Proving Ground, MD;* [5]*NIAID, NIH, Bethesda, MD.*

Objective: In US Army women *C. trachomatis* (CT) may cause a significant degree of morbidity. We sought to assess the relative cost-effectiveness of three screening and treatment strategies for CT in a military setting.

Methods: We compared universal and targeted screening to mass therapy with azithromycin for CT in female recruits using a cost-effectiveness analysis. At Fort Jackson, SC 7,191 recruits presenting for basic training from 1/96-3/97 were tested by urine LCR for CT. In a decision model from a military perspective, we assessed the total costs (program, medical, and military) and the level of prevented disease due to CT (PID, chronic pelvic pain, and ectopic pregnancy) associated with each of the 3 strategies. Results were extrapolated to an annual cohort of 13,236 recruits.

Results: The recruit sample had a CT prevalence of 9.56% and a diverse ethnic and geographical background. Approximately 86% were ≤ 25yrs old.

Strategy n = 13,236	Projected Costs (US$1995)		Projected PID (#) (silent &symptomatic)
	Program	Sequelae	
No Intervention	———	$973,100	316
Screen _25 yrs & Treat (+)	$120,600	$273,000	89
Screen All & Treat (+)	$137,900	$236,400	77
Mass Therapy	$207,400	$138,600	45

Mass therapy dominated both screening strategies, costing ~$16/woman and saving $627,100 over a projected 5 year period (8.2% and 4.9% more than targeted and universal screening, respectively).

Conclusion: Mass therapy in a well defined cohort of young women with a high prevalence of CT would prevent sequelae, would likely decrease the number of discharges for medical reasons in the first 6 mos. of service, and

- one swab for cell culture on McCoy cell
- one swab for direct immunofluorescence (DF/ antibodies (Syva)
- one swab for detection of secretory IgA (rELI:

Results for IgA secretory : Secretory IgA antibo patients ; 11 of them belonged to group with prese to group 2 without CT presence (10,71 %).

In spite of technical difficulties the results satisfactory, they are present in 50 % of positive di treatment secretory IgA become negative in few w

P512 COST-EFFECTIVENESS OF URINE-BASED S *TRACHOMATIS* WITH LIGASE CHAIN REACTI

Marrazzo JM, Celum CL, White C, Handsfield HH. University of Department of Public Health, Seattle, Washington, USA

Objective: To compare the cost-effectiveness of strate young males for *C. trachomatis* (CT) using the ligase ch esterase (LE) assays on urine.

Methods: CT prevalence and LE performance were ob males (mean age, 16.2 y) recruited in non-STD clinic se urine LCR and LE. Decision analysis was used to asse universal screening with LCR, and LCR testing only if LE screening, treatment of uncomplicated CT in males and management of sequelae in untreated females. Baselin for spontaneous cure rates, loss to follow-up before treat PID in 25% of untreated females, and treatment with sing

Results: Of 5,400 subjects, 270 (5.0%) were CT+. LE se CT were 59% and 95%, respectively. The CT prevale became cost-effective vs. no screening was 3.5% (95% universal screening became cost-effective vs. no scree Use of LE reduced total LCR tests performed by 92%. R in a population of 10,000 males screened (values in pare

Screening Strategy	Total cost, 1995 USD	CT cases not cured
None	$196,833	681
Selective (LE+)	$151,345	236
Universal	$246,396	99

Conclusions: For asymptomatic young men outside ST LCR is cost-effective at CT prevalence ≥6%. Although L CT detection, its use can reduce the cost of a comprehe CT prevalence is <6%.

P514 PREVALENCE OF CHLAMYDIA TRACHOM URINE SAMPLES FROM ASYMPTOMATIC UGASE CHAIN REACTION (LCR) IN COMPA LEUKOCYTE ESTERASE TEST (LET).

Pedreira W. MD. (1), Abreu H. MD (2), Alvez M. MD (1), Ol (1), Anzalone L. MD. (3).
1)Ministry of Public Health(MPH) STDs reference Laborat 2)MPH, STDs Epidemiological Division, Uruguay. 3)Assistant of Clinical Laboratory Professor at Clinicas Ho

Objective : To determinate prevalence of C.T. infection in attending preventive Public Health facilities, by LCR in com

Methods : From December 1996 to April 1997 two populat asymptomatic, sexually active persons (205 men, 244 wo 20 years old, attending the Preventive Health Department asymptomatic pregnant women, age range 14-18, mean 1 Hospital. This was a randomized, anonymous study. First 30cc) were collected in a sterile container, refrigerated to 4 laboratory to be processed immediately or frozen at (-) 20 LCR was provided by Abbott Laboratories (LCX C.T) and manufacture instructions. LET Dipstick (Multistix Bayer) we sample for 2 seconds and read after 2 minutes as: -, +, ++

Results : LCR (+) results were 15/528 (2.8%), distributed i (3.4%), men 5/205 (2.4%) ; in group B 2/79 (2.5%). The pre according to age in group A : women 15 -20 years old 4% 20 years old 1.7%, 21-25 years old 3.4%. For women in gr LCR (+)) LET (-) 5/5 LCR (+), for men LET (+) 1/4 LCR (+), U sensitivity and specificity of LET was low in women (40%a

Conclusions : This is the first prevalence study for C.T. in Uruguay. There was no available non invasive test to stu with low prevalence of C.T infection. With urine LCR we fo infection in women between 15-20 years old (4%), as in th should not be used as screening in this kind of population are cost effective even in asymptomatic women in our co

O256 INITIAL FINDINGS FROM CHLAMYDIA PREVALENCE MONITORING NETWORKS IN FIVE CITIES, 1995-1996

Groseclose SL, Lafferty WE, Macaluso M, Kissinger P, Blythe MJ, Bolan GA. Centers for Disease Control & Prevention, Atlanta, GA, USA.

Objective: Characterizing chlamydia (Ct) epidemiology amid changing reporting laws, test technologies, and testing practices presents unique challenges. Traditional case reporting yields numerator data that are difficult to interpret. As an alternative surveillance method, we monitored Ct prevalence among women of reproductive age seeking clinical services in 5 U.S. cities in 1995-96.

Methods: Women 15-34 yrs of age who attended selected family planning (FP), STD, or adolescent clinics, or community health centers and received a pelvic exam were screened for Ct. Since various diagnostic methods were used, we adjusted clinic prevalence estimates by test sensitivity and specificity. Prevalence ratios (PR) with 95% C.I. were used to assess predictors of infection and linear regression (LR) was used to assess the relationship among clinic population characteristics, duration of public sector screening, and clinic prevalences.

Results: In all cities, women 15-24 yrs of age attending FP [PR 4.5(3.7-5.5)] and STD [PR 3.2(2.7-3.8)] clinics had higher prevalence than older women. Black women attending FP [PR 2.4(1.9-3.1)] and STD [PR 1.8(1.5-2.1)] clinics had significantly higher prevalence than white women in all cities. By LR and using clinic-specific adjusted prevalences in the 31 clinics as our outcome measure, we found significant associations between clinic prevalence and: population proportion aged 15-24 yrs (beta = 0.157, p = 0.002); STD clinic populations (beta = 0.052; p=0.02); and year(s) of public sector screening (-0.012; p=0.001) [R^2 = 0.62].

Conclusions: Young age was the strongest individual level predictor of higher prevalence, while sustained public sector screening was associated with lower clinic-based Ct prevalence. Prevalence monitoring can identify subpopulations of sexually-active women at increased risk for Ct to better target Ct screening and other prevention activities.

O258 CHLAMYDIA CONTROL IN UPPSALA, SWEDEN IS ASSOCIATED WITH A FALL IN ECTOPIC PREGNANCIES

Egger M,[1] Herrmann B,[2] Low N.[3]

1. University of Bristol, England, 2. University Hospital, Uppsala, Sweden, 3. King's College School of Medicine & Dentistry, London, England.

Objectives: To analyse time trends for detection rates of genital *Chlamydia trachomatis* (CT) infection and ectopic pregnancy (EP) among women in Uppsala County, Sweden between 1985 and 1995.

Methods: Rates of CT per 100 examinations and of EP per 1000 reported pregnancies were calculated for women aged 15-24, 25-34 and 35-45 years. CT rates were also calculated for one-year age bands in each calendar year. Poisson regression models were used to examine the strength of association between EP and an increase in the CT rate of 5 per 100 tests in the current year and up to five years previously.

Results: Decreasing trends in both CT and EP rates were observed in all age groups. In women aged 15-24 years the CT rate declined steadily from 16 to 4/100 tests, while the EP rate fell from 12 to 6/1000 pregnancies. In 25-34 year olds CT decreased from 6 to 2/100 tests and EP from 24 to 11/1000 pregnancies. CT and EP rates in women aged 35-45 years showed declining but less consistent trends. In the youngest women the risk of EP was most strongly associated with the current CT rate (rate ratio, RR 1.58, 95% CI 1.29-1.94). For 25-34 year olds the strongest association was with CT rates one year earlier (RR 1.71, 1.38-2.11). Amongst older women EP was associated only with the CT rate two years earlier (RR 1.76, 1.08-2.87).

Conclusions: Rates of both CT and EP in this population have declined substantially between 1989 and 1995. The findings suggest that widespread testing for, and treatment of, CT has resulted in a reduction in both acute infections and in the long term reproductive sequelae. The time lag between CT infection and EP appears to vary with age.

O260 SEROLOGICAL STUDIES ON WOMEN WITH PELVIC PAIN, WITH OR WITHOUT CHLAMYDIAL PLASMID DNA IN ENDOMETRIAL BIOPSY TISSUE.

Chernesky M[1], Luinstra, K[1], Sellors J[1], Schachter J[2], Moncada J[2], Caul O[3], Paul I[3], L.Mikaelian[4], B.Toye[5], J.Paavonen[6], J.Mahony[1]. [1]Hamilton, Canada, [2]San Francisco, USA, [3]Bristol, England, [4]Buenos Aires, Argentina, [5]Ottawa, Canada, [6]Helsinki, Finland.

Objectives - To compare results obtained with various antibody assays with cervical culture and upper genital tract histopathology on women with pelvic pain with or without *C. trachomatis* plasmid DNA in endometrial tissue.

Methods - PCR was performed on DNA extracted from fixed endometrial biopsy tissues of women with pelvic pain. Five antichlamydial antibody assays were performed measuring total antibodies or IgG, IgM and IgA classes on sera from 14 women with plasmid DNA as well as 31 without plasmid DNA in their biopsy. All had a cervical culture and a histopathological diagnosis.

Results - Accepting presence of plasmid DNA as the gold standard, no single test had total diagnostic accuracy. The best sensitivity and specificity occurred with the following assays: whole inclusion fluorescence (100% and 80.6%); microimmunofluorescence IgM (78.6% and 93.6%); heatshock protein-60 EIA (42.9% and 100%). Although the recombinant anti-lipopolysaccharide ELISAs measured antibody classes in a large proportion of these women, specificity was poor. The sensitivity and specificity was 28.6% and 100% for cervical culture, and 71.4% and 51.6% for endometrial histopathology. Analysis of patient serological profiles suggested that six women without endometrial chlamydial DNA may have been cases which were missed due to PCR inhibitors, or aberrant sampling.

Conclusions - Evaluations of serological assays to diagnosis *Chlamydia trachomatis* upper genital tract infections should use the presence of organisms

O257 OPPORTUNISTIC SCREENINGSPROGRAM FOR CT INFECTIONS IN AMSTERDAM, THE NETHERLANDS

Van den Hoek JAR, Mulder-Folkerts D, Coutinho RA, Buimer M, Dukers N, van Doornum GJJ , Municipal Health Service, Amsterdam.

Objective: by means of an opportunistic screeningsprogram to determine: i) the participation, ii) the prevalence of CT infections in the heterosexual asymptomatic populations, iii) the costs/benefits of such a program in comparison with a systematic screeningsprogram (see abstract Boeke et al.).

Methods: heterosexually active women and men (ratio 2:1), 15-40 years, consulting a general practitioner (GP), without symptoms of STD, are approached for screening for CT by LCR on urine. Of both participants and refusers only few (demographic) data are collected. In case of CT infected patients the GP is interviewed on treatment and partner notification. Study period: 5/96-5/97.

Results: results sofar relate to i) and ii). Results ad iii) will be available in October. By April 97, 3605 persons were eligible of whom 3393 (94.1%) participated. Men refused more often than women (9.1% vs 4.4%, $p < 10^{-6}$); refusers were somewhat younger than participants (29.0 vs 29.8, p=0.05). No relation was found with ethnicity or insurance. CT was diagnosed in 4.8% (113/2337) of the women and in 4.8% of the men (50/1051). Age and ethnicity were independent predictors for CT. So was the prevalence in black Surinam women 13.3% vs 3.9% in white Dutch women and in women age group 15-20 yrs 12.5% vs 2.4% in women of 35-40 yrs. Of 145 CT patients data were available regarding treatment and partner notification: all but 9 were treated mainly with azithromycin. In 86% partner notification was discussed by the GP, but mostly limited to one single partner only.

Conclusions: we found a high (94.1%) participation rate and prevalence of CT, particularly in Surinameses and younger age groups. Implications for large scale screening (?=opport./system./age/ethnicity) will be discussed.

O259 PREVALENCE AND INCIDENCE OF *CHLAMYDIA TRACHOMATIS* (Ct) USING URINE PCR SCREENING IN A PEER-BASED COMMUNITY-LEVEL INTERVENTION PROGRAM AMONG HIGH-RISK URBAN YOUTH

Rietmeijer CA, Yamaguchi KJ, Ortiz CG, LeRoux T, Ehret JM, Judson FN, Douglas JM. Denver Public Health Department, Denver, CO, USA.

Objective: To describe the prevalence and incidence of Ct among high-risk urban youth enrolled in a community-level STD prevention program.

Methods: Through a peer network referral system, youth at high risk for STD in inner-city Denver were recruited for urine Ct screening by polymerase chain reaction (PCR). Urine samples were collected in field (streets, parking lots, parks, peer's homes) and facility (schools, recreation centers) settings. Samples were transported to the local health department and tested by PCR. Male youth testing positive for Ct were contacted and treated in the community by program outreach workers. Ct positive women were referred to local clinics for comprehensive STD examination and treatment.

Results: To date, 820 Ct PCR urine tests have been performed, 662 of which were first-time tests, and 158 were repeat tests. Ct prevalence among first-time testers was 7.5% (50/662). Prevalence was similar among men (42/553, 7.6%) and women (8/109, 7.3%), but significantly higher in field settings than in facility settings (10.8% vs 4.3%, p<0.01). Among repeat tests, 108 were among participants who tested Ct negative on the first test. Of these, 8 (7.4%) were positive after a mean of 8.3 months of follow-up, for an incidence density of 0.11/per person-year of follow-up (95% confidence interval: 0.09-0.13). Of 58 individuals with positive Ct tests, 56 (96%) were traced back into the community and treated by outreach workers or referred for clinical follow-up and treatment.

Conclusion: Ct prevalence among sexually active urban youth is high and more than 10% in this group are likely to acquire Ct every year. In addition to delivering STD screening and treatment services to a largely asymptomatic group of high-risk youth, shown to have great difficulty in accessing traditional clinic-based STD services, this type of community-level intervention appears to be a promising mechanism to study epidemiological trends of Ct in this population.

O261 POOLING URINE SAMPLES FOR THE SCREENING OF *CHLAMYDIA TRACHOMATIS* IN WOMEN BY LIGASE CHAIN REACTION (LCR): ACCURACY AND COST-EFFECTIVENESS

Kacena KA[1], Howell MR[1], Quinn TC[1,2], Gaydos CA[1] - [1]The Johns Hopkins University, Baltimore, MD; [2]NIAID, NIH, Bethesda, MD, USA.

Objective: The accuracy and cost-effectiveness of pooling urine samples for the detection of genital *C. trachomatis* infection by LCR (Abbott) was examined. A model to determine the number of samples to be pooled for lowest cost at various population prevalences was developed.

Methods: 284 samples were pooled by 4 into 71 pools and 200 samples were pooled by 10 into 20 pools. All 484 samples pooled were also tested individually. The volume of each sample per assay was 100ul for the unpooled assays, and 25ul and 10ul for the pools of 4 and 10, respectively. The cut-off ratio for the individual samples was 1.0, but was reduced to 0.2 in the pooled assays following preliminary testing. In the model, the binomial distribution was used to predict the percentage of pools with at least one positive sample. The estimated cost per sample included the cost of the technician, laboratory consummables, and the assay costs from pooling the samples and then retesting samples in positive pools individually.

Results: Pooling up to 10 samples was found to be 100% sensitive. One of 43 all negative pools of four (2.3%) tested positive with a cut-off ratio of 0.24; however, since all of the samples in pools which test positive are retested individually, no accuracy was lost by using the pooling protocol. In a population with 8% genital *C. trachomatis* prevalence, pooling samples by four would reduce the assay cost including technician time from $12.76 to $8.54 per sample, reducing the cost by 33%. The model demonstrated that with lower prevalences, pooling from 4-10 samples can reduce the cost per sample by 40-64%

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A multicentric descriptive study was done. It involved 274 patients, both male (71 - 21.91%) and female (20[illegible] - 74.09%). Average age was of 34 years (minimum 15 years - maximum 83 years). This 274 patients reported 1005 symptoms and signs with an average of 3.66 symptoms or signs per patient. 221 patients (80.66%) were evaluated as total recovery of the symptoms and 53 patients (19.34%) persisted with at least one clinical manifestation. It is important to mention that in 5 of this 53 patients new symptoms appeared in the second visit ; this symptoms were not reported in the first medical evaluation.

Adverse effects were observed in 20 patients (7.3%) but only in 3 cases (1.09%) the medication was suspended.

This evaluation shows that patients with non gonococcic genitourinary infections present a good response to therapy with Roxithromycin. Besides, side efects are very low with this therapy. Adverse effects are considered not serious and Roxithromycin rarely has to be discontinued.

ICMASK 98
Barcelona, Spain

7

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8.09 Single-dose Azithromycin (AZ) for Mass Therapy to Control *Chlamydia trachomatis* (CT) in Female Army Recruits: a cost-effectiveness model

HOWELL MR[1], QUINN TC[1,2], HENDRIX R[3] MCKEE K[4], GAYDOS J[5], GAYDOS CA[1*]

[1]*The Johns Hopkins Univ., Baltimore, MD;* [2]*NIAID, NIH, Bethesda, MD* [3]*Fort Jackson, SC* [4]*Fort Bragg, NC,* [5]*Jackson Foundation, Rockville, MD.*

Objective: There is a high preyalence of *C. trachomatis* (CT) in female U.S. Army recruits, which may cause serious morbidity due to PID. We evaluated the cost-effectiveness of treating all recruits with AZ to prevent chlamydial sequelae compared to testing all recruits and treating only those with positive CT tests.

Methods: In a decision analysis, we modeled mass treatment and universal testing to determine the incremental cost-effectiveness of these two strategies. From a military perspective, we calculated the total program costs, the projected costs of lost training, the projected costs of sequelae due to CT, the projected level of prevented disease (PID, chronic pelvic pain, and ectopic pregnancy) and the projected number of military discharges for medical conditions. 9,192 recruits presenting for basic training at Ft Jackson, SC 1996-97 were tested by urine LCR to determine CT prevalence. Results were extrapolated to a hypothetical population of 10,000 recruits per annual cohort.

Results: The recruit sample had a CT prevalence of 9.0%. 218 cases of PID would be expected in the absence of a control program. Mass therapy would prevent 187 cases, 21 more than universal testing. Mass therapy saved $39,500 over universal testing for a 5-yr follow-up period and $357,300 over no program. At CT prevalence > 6.2% and fewer than 14.1 clinic visits per 100 individuals for moderate to severe side-effects, mass therapy provided a cost-savings over universal testing. Both strategies provided cost-savings over no program at CT prevalences over 3%.

Conclusion: Mass therapy would prevent sequelae, would likely decrease the number of military discharges for medical reasons in the first 6 mo. of service, and would save overall costs relative to universal testing. Mass therapy could be considered as a first line of control for chlamydia in a well-defined cohort of young women with a high prevalence of CT.

dom use was noted in persons who received more recent positive test results than among persons with positive test results from earlier years ($p<0.001$), though this trend was not noted in heterosexual men. The proportion of persons who injected drugs [IDU] decreased with more recent years of first positive HIV test [$p=0.013$], especially among women. There were slight decreases in the proportion of persons who traded sex for money or drugs, and who used cocaine, with more recent years of first positive HIV test, but the proportion using crack increased. **Conclusions:** High-risk practices, such as sex without condoms and IDU, have decreased among MSWM and women. Heterosexuals are emerging as a more prominent group for HIV infection.

P-12.3 The Structure of a Newly Identified Genetic Subtype in the Hiv-1 Epidemic in Africa. J.K.CARR, F.E. MCCUTCHAN, M. EMERSON, D.BIRX. Henry M. Jackson Foundation for the Advancement of Military Medicine, Division of Retrovirology, Walter Reed Army Institute of Research, Rockville, MD.

Objective: Genetic analysis of HIV-1 genomes has led to the description of at least 10 different genetic subtypes, each with its own geographic or demographic distribution. Although subtype A is one of the most common genetic subtypes of HIV-1 in Africa, only three full-length genomes of this subtype have been sequenced: two from Uganda and one from Nigeria. **Methods:** Two isolates, DJ263 and DJ264, characterized as subtype A by gag and env sequencing, have been cloned and sequenced in full for the first time. The entire genome was sequenced except for a 73 nt region in the LTR. These subtype 'A' viruses were from Djibouti, on the coast of East Africa. Phylogenetic analysis of the full-length genome was performed with these new isolates. **Results:** The Djibouti viruses were found to form a unique cluster in the full-length analysis, grouping with previously sequenced isolate, IbNG, from Nigeria. They were distinct from subtype A and similar to each other from the 5' to the 3' end. Detailed analysis of the subtype structure of these isolates in comparison with reference sequences of the main HIV-1 sutypes, revealed them to be complex recombinants between subtypes A, G and an original "IbNG" parental strain. Both Djibouti isolates and the Nigerian isolate had the same complex subtype structure. **Conclusions:** Full- length genomes from one of the common subtypes in Africa will be fully characterized in this report. Although related to subtype A in both gag and env, the isolates were found to be a homogeneous viral subtype of their own, with a complex subtype structure recombinant between two known subtypes, subtypes A and G, and one unknown subtype, the putative parental subtype . It is recommmended that this viral subtype be given the new subtype designation of 'IbNG*'. Like the subtype E* viruses, which are E/A recombinants, this subtype has a segment from an original parental virus, a virus which has never been found in its 'pure', or non-recombinant, state.

Board 31

P-12.4 A Silent Epidemic of *Chlamydia trachomatis* Genital Disease in Female U.S. Army Recruits. CA GAYDOS, MR HOWELL, KL CLARK, KT MCKEE, RM HENDRICKS, D ELLIS, TC QUINN, JC GAYDOS. Johns Hopkins Univ., Baltimore, MD, Walter Reed Army Inst Res, Washington, DC, Ft. Bragg, NC, Ft Jackson, SC, NIAID, NIH, Bethesda, MD, HM Jackson Fndn, Rockville, MD.

Background: *C. trachomatis* (CT) infections in the U.S. exceed 4 million cases annually, occur mostly in the young and lead to costly sequelae (PID, ectopic pregnancy, and infertility). Most (>80%) infections are asymptomatic in women, leading to epidemic rates in sexually active youth. Our hypothesis was that a large epidemic of treatable CT genital infections, related to the ongoing civilian epidemic, was occurring in female recruits. **Methods:** Ligase Chain Reaction (LCR) of urine specimens was used to determine the prevalence of CT infections in female military recruits (N =9,192) at induction. Demographics and sexual risk data were collected. **Results:** Overall prevalence was 9.0%. By questionnaire, 93.6% reported vaginal sex, 26% had >1 sex partner and 30.5% had a new partner. Only 15.5% always used condoms. By age, prevalences were: 11.0% (17-20 yr), 8.0% (21-25 yr), 3.1% (26-30 yr), 1.9% (31-35 yr). By home state, 4 states had a prevalence >15%, 8 states 10-15%, and 12 states 5-10%. By multivariate analysis, significant variables associated with CT positivity were vaginal sex (OR 4.1), young (17-25 yr) age (OR 3.4), African American (OR 2.7), > 1 partner (OR 1.4), and a new partner (OR 1.5). A model consisting of LCR screening young female recruits (17-25 yr) would test 87.2% of the recruit population and identify 95.8% of CT positives. **Conclusions:** A high prevalence of CT infection exists in female army recruits, especially those of young age. Differences by state may be representative of national, geographically diverse prevalences. Detection of infection by LCR of urine permitted a large, efficient screening program. Data collected are being used to develop a cost-effective treatment program.

P-12.5 Epidemiology of Shigellosis in San Francisco during the HIV Era. J. T. BAER, D. J. VUGIA, A. L. REINGOLD, T. ARAGON, F. J. ANGULO and W. Z. BRADFORD, for the CA Emerging Infections Program. CA Emerging Infections Program, CA Department of Health Services, UC-Berkeley School of Public Health, Berkeley, CA; Centers for Disease Control and Prevention (CDC), Atlanta, GA; San Francisco Department of Public Health, UC-San Francisco.

Objective: The impact of HIV infection on the epidemiology of Shigellosis and its potential role as a risk factor have not been well described. To better understand this relationship and to assess the role of gay sex, a recognized risk factor for Shigellosis, we conducted an investigation of cases of Shigellosis in San Francisco, a city with a high prevalence of both HIV infection and men engaging in gay sex. **Methods:** As part of CDC's Emerging Infection Program, active surveillance for infections caused by *Shigella species* was conducted in SF during 1996. All available medical records were reviewed using a standardized data collection instrument and data previously collected by the SF Department of Public Health (DPH) during routine interviews of cases were obtained. The estimated prevalence of HIV infection and men engaging in gay sex was obtained from the SF DPH. **Results:** A total of 228 culture-confirmed cases were identified, including 142 and 73 caused by *S. sonnei* and *S. flexerni*, respectively. The incidence rate in cases per 100,000 population was 31.5, compared with an active surveillance rate of 10.9 in neighboring Alameda County (AC) and a reported rate of 7.3 in the U.S.. The incidence rate in the 25-44 year age group was 46.0 cases per 100,000 population, compared with 6.8 cases per 100,000 population in AC, and the rate in HIV-infected persons was 442 cases per 100,000 population. Adult cases (age > 17 years) comprised 80% (181/228) of the total, and had the following characteristics: male gender (75%), white race (70%), gay male (65%), HIV-infected (52%), and sexually active in the 10 days prior to interview (69%). Fifty-one percent (96/190) of infections occurred in gay, adult men. When compared to the non-gay and non-HIV infected population, the incidence rate ratios for the gay and non-HIV-infected, the non-gay and HIV-infected, and the gay and HIV-infected populations were 4.8 (95% Confidence Interval (CI) 2.7-8.0), 34.0 (95% CI 14.2-70.1), and 35.0 (95% CI 24.6-49.5), respectively.
Conclusions: These population-based data demonstrate high overall rates of Shigellosis and dramatically elevated rates in HIV-infected persons. The high prevalence of HIV infection and men engaging in gay sex are likely important determinants of the Shigellosis rates in SF. The relative contribution of behavioral factors as compared to compromised host immunity in HIV-infected individuals warrants future investigation.

- AGENDA -

ARMED FORCES EPIDEMIOLOGICAL BOARD

NAVY ENVIRONMENTAL HEALTH CENTER
2510 Walmer Avenue
Norfolk, Virginia 23513-2617
16 - 17 April 1998

Gerald F. Fletcher, M.D., President
Col Vicky L. Fogelman, USAF, BSC, AFEB Executive Secretary

Thursday, 16 April 1998

0730	Sign In	
0745	Welcome/Administrative Announcements	Dr. Fletcher COL Fogelman
0800	Command Brief	CAPT Macys
0830	Comparison of Licensed Hepatitis A Vaccines (Follow up)	CDR Bryan
0900	Update on Interchangeability of Two U.S. Licensed Hepatitis A Vaccines (Follow up)	Dr. Kuter
0930	BREAK	
0945	Cost Effectiveness of G-6-PD Testing (Follow up)	CAPT Littrell
1015	Chlamydia Trachomatis in Female U.S. Army Recruits	Dr. C. Gaydos
1045	DoD Influenza Surveillance Plan	MAJ Fisher
1115	Upper Respiratory Infections on Collective Protection Systems Ships	CAPT Thomas
1145	LUNCH	
1300-1630	Tour of Naval Amphibious Assault Ship	

Introduction

C. trachomatis infections exceed 4 million cases in the U.S. annually. 70% are asymptomatic in women who often remain undiagnosed, resulting in endometritis, PID, ectopic pregnancy, and infertility. Infections are highest in young, sexually active persons.

Costs of infections and sequelae have been estimated at $5 billion annually.

Molecular amplification techniques such as LCR are highly sensitive and specific for use with easily obtainable and non-invasive urine specimens.

A comprehensive study among young military women has never been performed; a prevalence and risk factor investigation of Army females was instituted using the LCR assay and a questionnaire.

Methods

Inprocessing female recruits at Ft. Jackson, SC were asked to volunteer for the study by a civilian nurse. Females with gynecologic complaints at a TMC (Ft. Jackson) and women attending Pap clinics (Ft. Bragg) were similarly enrolled.

Volunteers signed a consent form, provided a urine specimen, and answered a demographic and sexual history questionnaire. Once monthly, recruit nonvolunteers were asked to complete the study questionnaire anonymously.

Specimens and questionnaires were processed and tested at Johns Hopkins University. Urines were tested by Ligase Chain Reaction (Abbott Laboratories, Abbott Park, IL). Data was entered using Scantron Corporation (Tustin, CA) forms.

LCR results, demographics, and risk factor information were analyzed using standard statistical methods (Stata, College Station TX).

Recruit Population, Demographics (%)

volunteer rate = 66.2%

overall chlamydia prevalence = 7.3%

Variable	Volunteer (%) n = 3,177	Nonvolunteer (%) n = 400	p-value
<25 years of age	86.1	96.8	0.09
African American	34.5	33.5	0.68
Prior Chlamydia	9.4	2.3	0.00
Vaginal Sex	93.5	69.8	0.00
New Sex Partner	25.4	17.8	0.00
>1 Sex Partner	23.3	18.0	0.02
Never Use Condoms	77.2	53.8	0.00

Recruit Population
Univariate Analysis
n = 3,177

Variable	O.R.	95% C.I.
<25 years of age	3.1	1.73 - 5.64
African American	2.8	2.10 - 3.82
Vaginal Sex	2.7	1.18 - 6.13
New Sex Partner	1.6	1.17 - 2.06
>1 Sex Partner	1.6	1.20 - 2.14

Recruit Population
Multivariate Analysis
n = 3,177

Variable	O.R.	95% C.I.
<25 years of age	3.0	1.68 - 5.51
African American	3.1	2.26 - 4.15
New Sex Partner	1.7	1.26 - 2.25

Active Duty Populations
Demographics (%)

Variable	TMC n=276 (volunteer rate 68%)	Pap n=171 (volunteer rate 50.7%)
<25 years of age	85.8	57.9
African American	52.4	57.1
Prior Chlamydia	12.2	17.1
Vaginal Sex	95.3	97.1
New Sex Partner	25.0	11.4
>1 Sex Partner	21.0	17.7
Never Use Condoms	66.9	86.9

Active Duty Populations
Prevalence (%) of Chlamydia

Variable	TMC n=276 Ct prevalence = 12.8%	PAP n=171 Ct prevalence = 8.0%
<25 years of age	13.4	10.1
African American	18.1	10.0
Prior Chlamydia	11.1	3.3
Vaginal Sex	13.1	8.2
New Sex Partner	9.5	15.0
>1 Sex Partner	11.3	9.7
Never Use Condoms	13.1	8.6

Army Chlamydia Study by urine LCR

Population	N	Prevalence (%)
New Recruits*	3,177	7.3
TMC*	276	12.8
PAP**	171	8.0

* Ft. Jackson, SC
** Ft. Bragg, NC

Conclusions

Urine based screening revealed a prevalence of 7.3% in female recruits, 12.8% in symptomatic women (TMC pts.), and 8.0% in Pap smear clinics.

Relevant risk factors upon which future screening of recruits could be based included young age, African American race, and a new sex partner.

High prevalences in symptomatic TMC and Pap clinic patients probably justifys routine screening for chlamydia in these populations.

This acceptable urine based method provided evidence that a routine screening program should be considered to prevent sequelae and their costs.

A comparison of "Wet"versus "Dry"vaginal swab transport conditions for the detection of Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (NG) using the AMPLICOR CT/NG PCR test

C. A. Gaydos, [1]* K. A. Crotchfelt, [1] B. Pare, [1] T. C. Quinn, [1,2] K. T. McKee, [3] M. Tennant, [3] A. M. Rompalo, [1]

1. The Johns Hopkins University, Baltimore, MD; 2. NIAID, NIH, Bethesda, MD, 3 Fort Bragg, NC

REVISED ABSTRACT

Vaginal swabs, which can be self-administered, have been found to be both sensitive and specific in detecting CT and NG using polymerase chain reaction (PCR). As part of an on-going study of U.S. Army women attending a military STD clinic, paired vaginal specimens and paired cervical swabs were collected from 472 consenting women. We compared the sensitivity for detection of CT and NG from vaginal swabs that were shipped dry to that from vaginal swabs that were shipped ("wet") in the standard Roche (Branchburg, NJ) Specimen Transport Medium (STM). PCR results were also compared with an enzyme immunoassay test (EIA) for CT and culture for NG from cervical swabs, both performed at the military hospital laboratory according to standard procedures. Vaginal specimens were shipped to Johns Hopkins to arrive within 4 days of collection. Upon receipt, the "dry" swab was put into the STM and processed in the manner recommended by the manufacturer. PCR (Roche) was performed for CT and NG on both "wet" and "dry" specimens. Discordant specimens were adjudicated by an additional cervical swab for PCR and ligase chain reaction (LCR). PCR-CT: "dry" vaginal swabs detected 50/472 (10.6%) vs. 53/472 (11.2%) for "wet", while EIA detected 41/472 (8.7%). PCR-NG: "dry" swabs detected 29/472 (6.1%) and "wet" swabs detected 27/472 (5.7%), while culture detected 13/472 (2.8%). After discrepant analysis, PCR of "dry" swabs was 94.3% sensitive and 100% specific for CT, while PCR of "wet" swabs was 94.3% sensitive and 99.5% specific. PCR-NG of "dry" swabs was 93.3% sensitive and 96.7% specific, while PCR-NG of "wet" swabs was 94.1% sensitive and 97.6% specific. Use of self-administered vaginal swabs that are shipped dry has great potential for the diagnosis of CT and NG by PCR, especially for military women, who may not have ready access to adequate or confidential health care facilities in a field environment.

CHLAMYDIAL INFECTIONS

Proceedings of the Ninth International Symposium
on Human Chlamydial Infection

Napa, California, USA
June 21 - 26, 1998

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NATIONAL GEOGRAPHIC VARIATION AND PREDICTORS OF *CHLAMYDIA TRACHOMATIS* INFECTIONS USING URINE LIGASE CHAIN REACTION FROM A LARGE STUDY OF YOUNG FEMALES WHO JOIN THE U.S. ARMY

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Introduction: Most *C. trachomatis* genital infections are asymptomatic in females, who are at risk of developing costly sequelae, such as pelvic inflammatory disease, infertility, and ectopic pregnancy [1-3]. Screening of young sexually active women, who may not attend health clinics, has been recommended [1,4]. With the development of highly sensitive DNA amplification methods for the detection of *C. trachomatis* infections using urine, a pelvic examination is no longer required to screen women at risk for chlamydia infections [5-7]. We screened young women new to the Army from across the U.S., using ligase chain reaction (LCR) of urine specimens to determine geographic variation in prevalence, to assess the ease and utility of this methodology, and to determine predictors of infection that could be useful in developing a control program.

Methods: Between January, 1996 and December, 1997, all incoming female Army recruits who were present at the Physical Examination Section, Reception Battalion, Fort Jackson, SC, on Sundays were offered voluntary participation in a urine-based chlamydia study, which was approved by the Institutional Review Boards of Johns Hopkins and the Army. After an educational briefing by a civilian research nurse, 13,211 women (volunteer rate 79.7%) joined the study. Demographic information, home state, and sexual risk history were recorded on a questionnaire. First catch urine specimens (20-30 ml) were collected by the volunteers. Questionnaires, consent forms, and urines were shipped to Johns Hopkins University Chlamydia Laboratory, where the LCR tests (Abbott Laboratories Abbott Park, IL) were performed according to manufacturer's instructions. Using LCR results, prevalences by home state

were determined. Other demographic data and risk factor information were analyzed as dichotomous variables. Univariate and multivariate logistic regression analysis were performed using Intercooled Stata 4.0 (Stata Corporation, College Station, TX).

Results: From 13,211 women, the prevalence of chlamydia infection was 9.2% From year one to year two of the study the prevalence increased from 8.5% to 9.7%. The median age was 21 years and 50.9% were Caucasian (prevalence 5.5%). 35.8% were African-American (prevalence 14.9%) and 13.3% were other races (prevalence 8.1%). By questionnaire, 93.0% reported having had vaginal sex and in the previous 90 days, 26.3% had more than one sex partner 30.9% had a new sex partner, and only 16.0% consistently used condoms Previous chlamydia infection was reported by 9.1%, gonorrhea by 3.3% trichomonas by 4.6%, and syphilis by 0.6%. 86.1% of women did not report a previous STD, but 1,028 (9.0%) of them were chlamydia infected.

Five states (South Carolina, Georgia, Alabama, Louisiana, and Mississippi) had prevalences of 15% or greater. There were 6 states (New Jersey, North Carolina, Kentucky, Texas, Oklahoma, and Arkansas) with prevalence 10% up to 15% and 17 states plus Puerto Rico with a prevalence 5% up to 10%. Five states demonstrated a prevalence of <5%. There were 3 states, 3 territories, and the District of Columbia from which <100 recruits were tested and prevalence was not calculated.

In univariate analysis, six significant risk factors were associated with chlamydia infection: young age (17-25 years), African American, ever having vaginal sex, more than 1 sex partner, new sex partner in the previous 90 days and lack of condom use. Prior diagnosis of a STD was not significantly associated with positivity. Condom use was not entered into the multivariate model a large number of recruits did not definitively provide results. multivariate analysis, independent predictors for chlamydia infection were vaginal sex (OR 5.7, 95% C.I. 3.3, 9.7), young age (OR 3.0, 95% C.I. 2.3, 4. African American race (OR 2.8, 95% C.I. 2.5, 3.8), more than 1 sex partner (OR 1.4, 95% C.I. 1.2, 1.7), and having a new sex partner (OR 1.3, 95% C 1.1, 1.5).

A simple model of using only young age as a risk factor upon which base a screening program would detect 95.3% of the infections while requiring screening 87.9% of the population. Other similarly sensitive models were more complex, requiring ascertainment of more risk factors and screening more the population.

Discussion: This survey detected a high prevalence of chlamydia infection in asymptomatic females entering the Army. Urine screening was highly acceptable and easy to implement. This study represents the largest nation-wide study of asymptomatic young women performed for chlamydia infection using urine samples and DNA amplification testing, which is non-clinic based. Prevalences were much higher for the southern states than have been previously reported by national statistics [8]. Lower regional prevalences have been reported by CDC for most of the states in which we found prevalences above 10% and 15%, but those studies were clinic population based and did not use the more sensitive DNA amplification tests [8]. In regions of the Pacific Northwest, where chlamydia control programs have been in place for some time, our prevalence rate of <5% accurately reflected prevalences reported by other studies [9,10].

Use of young age of 25 years or less as a screening criteria appeared to offer a simple method upon which to base a control program for this population. A limitation of the study in generalizing this recommendation to other populations is that women who decide to join the military may be different from those who do not.

In summary, a high prevalence (9.2%) of chlamydia infection was found in young females joining the Army, with wide geographic variation from state to state. Prevalences ranged from >15% for several states to <5% for others, perhaps reflecting local chlamydia control programs and/or local burdens of disease. Our national prevalences are the first to be reported using urine LCR and based on females not seeking health care. Institution of a control program based on screening those female recruits of young age has the potential to reduce prevalent disease, to prevent transmission to sex partners, and to prevent associated morbidity.

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B6

Chlamydia Among U.S. Female Army Recruits: The Role of Geography, Race, and Age

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Background & Rationale: Regional variations in *C. trachomatis* prevalence have been documented in clinic populations. Similar regional variations in non-health care seeking women have not been examined to determine the influence of confounding variables such as demographics. It is necessary to understand differences in populations from non-traditional settings from a diverse geographic perspective.

Objectives: To describe and assess the significance of regional variations and determine if these differences remain when controlled for race and age in a non-health care seeking military population.

Methods: From 1/96 through 12/97, we tested 13,204 female recruits by ligase chain reaction of urine for *C. trachomatis* infection upon entry to the U.S. Army. The impact of regional variations (CDC reporting areas: northeast, south, midwest, west and territories) on chlamydia prevalence among these women was analyzed by ANOVA. The effect of intervening factors (self-reported race and age) was assessed by logistic regression.

Results: An overall prevalence of 9.2% (1,219/13204) was observed. Home state records were available for 13,152. Women coming from the northeast had a chlamydia prevalence of 6.9% (146/2103); the south 11.9% (760/6381); the midwest 7.1% (167/2351); the west 5.6% (117/2100); and the territories 10.0% (21/211), ($F<0.001$). Region, African American race and young age (age # 25) were all independent predictors of infection. Women coming from the southern states were more likely (O.R. 1.5, 95% CI: 1.3- 1.7) to be positive for chlamydia than women coming from the other four regions. Conversely women in the west were less likely (O.R. 1.4, 95% CI: 1.1-1.7) to have a positive test than other women.

Conclusions: In non-health care seeking U.S. Army recruits regional disparities in chlamydia prevalence exist. Other national studies in non-health care seeking populations are necessary.

B6

The Case for Routinely Screening Young Adults: Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (GC)Urine Testing at a Public Hospital Walk-in Clinic

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Background and Rationale: The availability of the urine ligase chain reaction (LCR) test to diagnose GC and CT makes it possible to screen large numbers of persons noninvasively.

Objective: To determine the prevalence of GC and CT in persons 18-30 being seen for complaints not related to the genitourinary tract at the walk-in clinic at Charity Hospital in New Orleans to determine whether the yield is sufficiently high to warrant routine screening of general medicine clinic patients in that age group.

Methods: Between January and June of 1998, men and women between the ages of 18 and 30 years attending a public walk-in clinic for health problems not related to the genitourinary tract were asked to participate in screening for CT and GC by providing a urine specimen. A brief survey on condom use and getting medical treatment was administered. Treatment was provided at no cost.

Results: 143 persons were approached, and 108 (75%) agreed to participate. Participants were 81% African-American, 52% male, with an average age of 23 years. These characteristics were not different from those refusing to participate. The CT infection rate was 8.3%; for GC it was 2.2%. The CT infection rate was 8.9% and 7.7% in males and females respectively. Of the participants giving a history of having been tested for CT or GC within the past 12 months, 3/26 (11.5%) had a current infection.

Conclusion: These findings show that routinely screening persons between the ages of 18 and 30 in a general medicine clinic serving an inner city population is warranted. Asymptomatic persons in this age category should be included in community-based screening programs designed reduce the prevalence of these infections.

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Prevalence and Risk Factors of *C. trachomatis* Infection in Male Military Recruits Using Urine Ligase Chain Reaction (LCR)

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Chlamydia trachomatis urogenital infections in women are associated with significant morbidity, including PID, ectopic pregnancy and infertility. In a study of female Army recruits using urine ligase chain reaction (LCR, Abbott Laboratories, Abbott Park, IL), *C. trachomatis* was identified in 9.3% of women screened. The effectiveness of efforts to limit chlamydial infections in women may depend on the prevention of re-infection through simultaneous screening and treatment of men. We tested male recruits for *C. trachomatis* using urine LCR to determine prevalence and to assess potential screening criteria for *C. trachomatis* infection in men. Each recruit who volunteered to participate provided a urine sample and answered a questionnaire. Among 1,203 men screened, the prevalence of infection was 4.9%. The mean age was 19.8 (±2.61) years, 61.6% were Caucasian, 33.8% had more than one sex partner, and 36.7% had a new sex partner in the last 90 days. Only 21.2% of men reported using condoms regularly, and 2.6% reported having prior chlamydial infections. Of the men that tested positive, only 13.6% reported having symptoms. Risk factors that proved useful for predicting chlamydial positivity included: African-American race, more than one sex partner, and a new sex partner. Young age was not a risk factor, as it was for women. Urine LCR is a convenient and well-accepted method for screening large numbers of men, and may be useful in developing strategies for limiting the spread of *C. trachomatis* in the population.

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PREVALENCE AND RISK FACTORS OF *C. TRACHOMATIS* INFECTION IN MALE MILITARY RECRUITS: MULTIVARIATE ANALYSIS

JA Cecil, MD; MR Howell, Johns Hopkins University: JC Gaydos, MD, MPH, HM Jackson Foundation: KT McKee, MD, MPH, Ft. Bragg, NC: RM Hendrix, D.O., Ft. Jackson, SC: TC Quinn, MD, Johns Hopkins University, NIH, NIAID: CA Gaydos, DrPH, Johns Hopkins University

OBJECTIVES: To determine the prevalence and assess potential screening criteria for *Chlamydia trachomatis* infection in male military recruits, to help target future interventions.
METHODS: 1,203 male Army recruits volunteered to provide a urine sample and completed a questionnaire addressing demographic and behavioral characteristics, during inprocessing at Ft. Jackson, SC. Urine samples were tested for the presence of *C. trachomatis* using ligase chain reaction. Multivariate logistic regression was performed to access criteria for a screening program.
RESULTS: The volunteer rate was 80.9%. The prevalence of infection was 4.9%. The mean age was 19.8 years and 61.6% were Caucasian. Only 13.6% of infected men had symptoms. Independent risk factors predictive for being chlamydia positive included: African American race, having more than 1 partner in the last 90 days, and the presence of symptoms. Of 3.4% who were symptomatic, 19.5% were infected. Of asymptomatic men, 4.4% were infected. 3% of those reporting condom use were chlamydia positive.
CONCLUSION: A significant number of male Army recruits are infected with *C. trachomatis*, and the majority of these men do not have associated symptoms to suggest infection. These men may be less likely to seek appropriate medical attention, and may contribute to the transmission of chlamydial infections. Urine LCR is a convenient, noninvasive method for screening large numbers of men, and will be used to screen more recruits as part of this ongoing study. Additional data from future screening will be presented.

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#414

TARGETED SCREENING FOR GONORRHEA IN NORTH CAROLI

Fox KK[1,2], Haar M[3], Leone PA[3], Hoffman I[3], Owen-O'Dowd J[2], Privette A[2], and
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Background: Gonorrhea is prevalent in many areas of the United States, but declining rates necessitate examination of screening strategies to ensure efficient use of testing resources.
Objective: To develop criteria for targeted gonorrhea screening based on readily obtainable risk factors for gonorrhea among women in STD and family planning (FP) clinics.
Methods: In the North Carolina Infertility Prevention Project, standardized demographic and clinical information were collected on consecutive female patients at STD and FP clinics in 10 county health departments. With logistic regression, models were developed to identify >95% of gonorrhea cases using small groups of readily obtainable risk factors.
Results: Of 7,138 women, median age was 22 years, 47.3% were African-American and 43.7% were white. Gonorrhea was found in 1.3% of FP patients and 6.8% of STD patients, respectively. Excluding race as a screening criterion, FP criteria included 4 risk factors (age<20, OR 5.2; new partner in 3 months, OR 3.2; has children, OR 2.1; and absence of vaginal symptoms, OR 2.0) to detect 98.1% of cases while testing 73.3% of patients. STD criteria included 5 risk factors (5 age groups, OR for <18 years 4.8; >1 partner in 3 months, OR 1.8; has children, OR 1.4; student, OR 0.5; and contact to any STD, OR 4.9) to detect 97.8% of cases while testing 83.5% of patients.
Conclusions: Screening criteria can be developed to target gonorrhea testing in a high morbidity area, especially in FP clinics. Higher prevalence among STD clinic patients may limit the usefulness of--and the need for--targeted screening.

#415

POINT-OF-ENTRY *Chlamydia trachomatis* (CT) SCREENING IN YOUNG FEMALE SOLDIERS: WHO DERIVES THE BENEFIT?

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OBJECTIVES: Mass screening of young adults at entry to training (e.g. military) using urine-based DNA amplification assays provides a target for reducing health care costs associated with chlamydia (CT) infections. However, about 50% of recruits return to civilian life within 2 years and are managed in the non-military health care sector. Disparity therefore exists between the financing source for screening (military) and the spectrum of beneficiaries (all others).
METHODS: From 1996 through 1998, we offered urine screening for CT to female Army recruits at Fort Jackson, SC using ligase chain reaction. Of 18,360 volunteers tested, 1,727 had positive results for CT (prevalence = 9.4%). A decision analytic model was used to establish the cost-effectiveness of screening in this setting from a societal perspective. Cost factors included those of screening and treatment, military training, and costs of treatment and sequelae. Attention was paid to the distribution of costs and benefits between the military and non-military health care sectors, using a five year analytic horizon.
RESULTS: Screening a cohort of 10,000 new military recruits with a 9.4% prevalence would cost $193,500 and prevent 238 cases of pelvic inflammatory disease (PID), 43 cases of chronic pelvic pain and 19 cases of ectopic pregnancy. Our model projected a savings of $216,500 to the military and $387,900 to the non-military health care sectors.
CONCLUSIONS: Identification and treatment of CT in female military recruits reduces the burden of disease to the benefit of both military and non-military health care systems. Financing of point-of-entry screening programs in the military and elsewhere as a joint venture between the training sponsor and general public funding sources would provide a cost-effective prevention strategy.

#420

DECREASING HOSPITALIZATION RATES IN FEMALE U.S. ARMY RECRUITS ASSOCIATED WITH A SCREENING PROGRAM FOR *Chlamydia trachomatis* (Ct)

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Objective: In response to a crude Army hospitalization rate for pelvic inflammatory disease (PID) of 1.4% (compared to the national average of 0.3%), voluntary screening for genital Ct was initiated in female recruits at the largest basic training center. This follow-up study examined hospitalizations in a non-healthcare seeking cohort of female soldiers, comparing those who were screened with those who were not.

Methods: A cohort of 28,074 females entering the Army from January 1996-December 1997 (7,053 volunteered to be screened and treated if positive, and 21,021 were not screened) were followed for subsequent hospitalization through March 1998. Rates were calculated as hospitalizations per person-year (PY). ICD9 codes 614 and 615 were used to identify PID hospitalizations.

Results: The race distribution between the screened (Ct prevalence of 9.1%) and unscreened groups was comparable; 85% (5,960) of those screened and 80% (16,704) of those unscreened were <25 years of age ($p<0.0001$). The hospitalization rate for PID was 4.2 /1,000PY in those screened and 4.5/1,000PY in those not screened ($p=0.75$). The rates for any hospital admissions were 18.1/1,000PY in those screened and 21.7/1,000PY in those not screened ($p<0.0001$).

Conclusions: Ct prevalence and PID hospitalization rates in the Army are high and a screening program was associated with a decrease in PID hospitalizations. The absence of statistical significance may be due to the use of inpatient data only, those screened being younger (a risk factor for Ct) than those unscreened, or possible behavioral or risk bias in the unscreened group The observed relationship of Ct screening on overall hospitalizations is being evaluated.

#421

LIMITED SCREENING AT INTAKE DOUBLES *CHLAMYDIA TRACHOMATIS* (CT) CASE DETECTION IN WOMEN AT COUNTY JAIL

Kent CK, Kohn RP, Klausner JD, Goldenson J. San Francisco Dept. of Public Health, CA, USA.

Background: Screening for CT in women >48 hours after intake into the San Francisco County Jails has been in place since 11/96. However, since more than 60% of women who enter the jail are released in <24 hours, a substantial number of women are not screened.

Objective: To compare the prevalence of CT between intake and post-intake county jail screening and to evaluate correlates of CT infection in women screened at intake.

Methods: Between 8/98 and 1/99, women were screened for CT at the jail intake facility 6 night shifts per week. Urine specimens were tested using LCx (Abbott Laboratories). Demographic and behavioral data were collected during specimen collection. Results were compared with characteristics of women screened at post-intake facilities during the same time period and for 1998 as whole.

Results: The prevalence at intake screening was 8.8% (58/659) and 7.0% (43/616) at post-intake screening (P=.22). The number of women screened at post-intake remained stable between 1/98-12/98 (average 105/month), even after addition of limited intake screening. Intake screening identified 58 additional cases, doubling the number of CT cases detected during time period. Approximately 90% of cases identified at post-intake received treatment and 50% of cases from intake screening receive treatment. Correlates of CT infection at intake screening included age <25 years (OR=3.4 [95%CI 2.2-5.6]), ≥ 5 partners last 6 months (OR= 5.6 [0.6-128]), and having received money/drugs for sex last 6 months (OR=2.0 [0.9-4.5]).

Conclusion: Limited CT screening (48 hours/week) incorporated into women's intake process in San Francisco County Jails significantly increased the number of detected and treated cases of CT infection in this high risk population.

HOSPITALIZATION RATES IN FEMALE U.S. ARMY RECRUITS ASSOCIATED WITH A SCREENING PROGRAM FOR *CHLAMYDIA TRACHOMATIS*

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Revised Abstract

Objective: The crude Army hospitalization rate for pelvic inflammatory disease (PID) during 1991-1993 was 1.4%, with a national average of 0.3% (1988). We examined hospitalizations in non-healthcare seeking female recruits who volunteered for testing for genital *Chlamydia trachomatis* (Ct) at the largest Army training center. The comparison group was women entering the Army during the same period who were not tested.

Methods: 28,074 females entering the Army from January 1996-December 1997 (7,053 were tested for Ct and treated if positive, and 21,021 were not screened) were followed for hospitalizations through December 1998. Hospital admissions were calculated per person-year. Adjusted relative risks (RR) were determined.

Results: The race distribution between the screened (Ct prevalence of 9.1%) and unscreened groups was comparable; 85% (5,960) of those screened and 80% (16,704) of those unscreened were <25 years of age (p<0.001). The RR of hospitalization for PID was 0.91 (95%CI 0.66-1.25) in those screened. The RR of hospitalization for any reason was 0.92 (95%CI 0.87-0.96) in those screened. Among women screened, there was no difference in PID hospitalizations between those positive for Ct and those who were negative on testing.

Conclusions: A Ct intervention program was associated with significantly fewer total hospitalizations in those screened. Ct positive women, identified by screening and treated, had hospitalization experiences similar to those who tested negative.

Chlamydia trachomatis (Ct) Infections in Female Army Recruits

- 13,204 female recruits (the Fort Jackson Study Group) were informed about sexually transmitted diseases and tested for Ct using DNA amplification (ligase chain reaction, LCR) of urine.
- Prevalence of *C. trachomatis* = 9.2%.
- Women testing positive were treated with 1g oral azithromycin.
- Independent risk factors of *C. trachomatis* infection = African American race and young age.*
- A positive test for *C. trachomatis* was associated with the presence of behavioral risk factors.*

*Gaydos, et al. NEJM 1998;339.

Hospitalization Study Objective

- To assess the impact of a screening program for *C. trachomatis* by measuring subsequent hospitalizations for sequelae.
- Among those "Screened", "Positives" were compared to "Negatives"; and all "Screened" women were compared to those "Unscreened".

Methods

- 53.4% (7,053) of 13,204 Fort Jackson Study Group women entered full-time active duty from January 1, 1996 to December 31, 1997. These 7,053 women comprise the "Screened" group.
- The "Unscreened" group consists of 21,021 females entering the Army on full-time active duty during the same time period who were not tested for *Chlamydia trachomatis* (Ct).*
- Using Army medical data sources, women hospitalized from January 1, 1996 through December 30, 1998 were identified. The maximum follow-up time was 3 years.
- Controlling for age, race, education, and aptitude score, relative risk of hospitalization was determined using Poisson regression,.

*Includes those who received a STD education class but did not volunteer for testing.

Study Populations

	Screened (n = 7,053)	Unscreened (n = 21,021)	p-value
<25 yrs of age	5,960 (85%)	16,704 (80%)	0.001
African American	2,501 (35%)	7,657 (36%)	0.350

Study Outcomes*

- Counts of hospitalizations for PID
- Counts of hospitalizations for ectopic pregnancy
- Counts of hospitalizations for infertility
- Counts of hospitalizations for PID, ectopic pregnancy, and infertility ("Combined")
- Counts of hospitalizations for any reason

*Reported per 1,000 person-years (P-Y).

Common Reasons for Hospitalization
(% of all hospitalizations for each group*)

	Screened(%)	Unscreened(%)
Pregnancy	41.4	42.6
Neurotic/personality	12.2	9.6
Injuries	4.9	5.4
Other diseases due to viruses	4.1	3.0
Acute Respiratory Infection	4.0	3.7
All sequelae (PID/ectopic/infertility)	3.0	3.0

*Using ICD9 categories.

Subsequent Hospitalizations*
Counts per 1,000 P-Y (actual counts)

	Screened (n = 7,053)	Unscreened (n= 21,021)
PID	4.6 (50)	5.1 (175)
Ectopic Pregnancy	2.6 (28)	1.9 (70)
Infertility	<0.01 (2)	<0.01 (9)
Combined Sequelae	7.2 (78)	6.8 (232)
All Hospitalizations	199 (2,163)	224 (7,598)

Relative Risk of Hospitalization
"Screened" vs "Unscreened"

	Unadjusted RR (95%CI) p	Adjusted* RR (95%CI) p
PID	0.91 (0.66-1.25) ns+	0 .94 (0.69-1.29) ns
Ectopic Pregnancy	1.33 (0.85-2.08) ns	1.39 (0.89-2.17) ns
Infertility	NA	NA
All Sequelae	1.06 (0.82-1.37) ns	1.1 (0.85-1.43) ns
All Hospitalizations	0.92 (0.87-0.96) .001	0.94 (0.90-0.99) .02

*Adjusted for age, race, education, and aptitude score.
* ns=not significant (p>0.05).

Hospitalizations for PID and Ectopic Pregnancy in "Screened" soldiers, by LCR result
Count per 1,000 P-Y (actual count)

	"Screened" Group (n=7,053) Chlamydia Positive	Chlamydia Negative	p-value
PID	7.1 (7)	4.4 (43)	0.230
Ectopic	1.0 (1)	2.7 (27)	0.307

Study Limitations

- Behavioral risk factors were not available for the "Unscreened" group.
- Outpatient data are incomplete and were not analyzed.
- Diagnoses were based on reported ICD-9 codes, but not verified by chart review.

Conclusions

- Being screened for *C. trachomatis* was associated with a subsequent decrease in all hospitalizations.
- There was no difference in hospitalizations for PID, ectopic pregnancy and infertility between the "Screened" and "Unscreened" populations, but risk factors for infection in the "Unscreened" group are unknown.
- Of the women participating in the screening intervention, those testing positive and receiving treatment had the same PID and ectopic pregnancy experience as those testing negative.

OVERVIEW OF *CHLAMYDIA TRACHOMATIS* INFECTIONS AMONG INITIAL ENTRY TRAINING SOLDIERS

Investigators:

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Joel C. Gaydos, M.D., M.P.H.

Thomas C. Quinn, M.D.

Charlotte A. Gaydos, Dr. P.H., M.P.H.

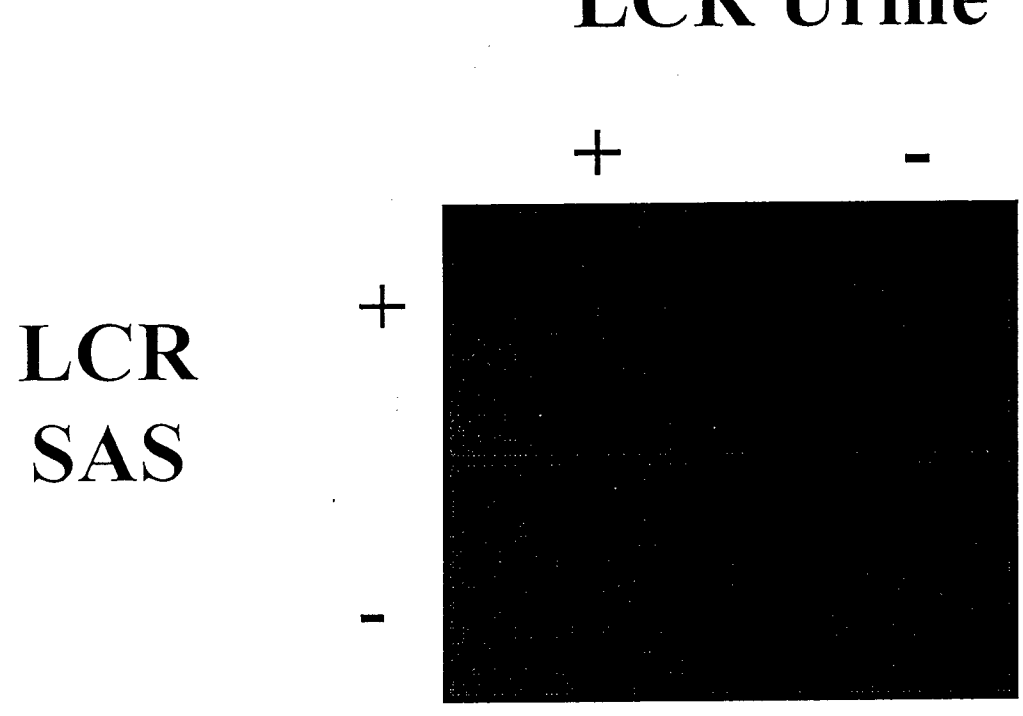
COMPARISON OF SELF ADMINISTERED SWABS AND URINE FOR THE DETECTION OF CHLAMYDIA TRACHOMATIS GENITAL INFECTIONS IN NON-HEALTH CARE SEEKING MILITARY WOMEN

Gaydos, CA.[1], Howell, MR.[1], Tawes, J.[1], Theodore, M.[1], Gaydos, JC.[2], McKee, KT.[3], Rompalo, A.[4], Syffus, P.[4], Lindner, J.[5], Quinn, TC.[1,5]

1. The Johns Hopkins University, Baltimore, MD, 2. DOD Global Emerging Infections System, 3. Fort Detrick, SC, 4.Ft. Jackson, SC, 5. NIAID, NIH, Bethesda, MD,

Background: Self-administered vaginal swabs (SAS) for the detection of *C. trachomatis* using nolecular tests have been reported to be sensitive alternatives to urine specimens or clinician-collected cervical swabs. From March - August, 1999, in a study of *C. trachomatis* in women who ecently joined the U.S. Army, we compared SAS to urine specimens using the ligase chain eaction test. Methods: Women (3419) were asked to provide a urine specimen and/or to provide n SAS. The volunteer rate was 92.4% (3159) for providing any specimen. "Wet" transport was sed for 931 SAS and "dry" transport was used for 1096 SAS. There were 2009 matching urine nd SAS specimens. For a 2 week period, participants were asked to provide which ever specimen hey preferred. All other weeks, women who provided a urine specimen were also asked to provide n SAS. Results: The prevalence of chlamydia for all volunteers using any specimen was 13.8%.)f 2009 paired urine and SAS specimens, there were a total of 209 (10.4%) positive urine pecimens; 180 (8.9%) positive by SAS; 157 (7.8%) positive for both urine and SAS; and 1777 egative by both specimens. There were 52 specimens positive by urine testing and negative by AS, while 23 were urine negative and SAS positive. Using the urine test as the gold standard, the ensitivity of SAS was 75.1% (157/209) and the specificity was 98.7% (1777/1800). There was no tatistical difference for sensitivity of swabs transported "wet" as compared to those shipped dry". Of those with matched specimens, approximately 60% of women stated a preference for ollecting urine specimens. During the 2 week preference period where individuals could provide ither a urine or an SAS, 93% provided urine, 6.7% provided SAS, and 0.2% provided both. Conclusions: In predominantly asymptomatic women, SAS were not as sensitive as urine pecimens for the detection of *C. trachomatis*. There was little difference in specimen collection reference when 2 specimens were collected but given a choice, women preferred to collect a urine.

RESULTS Table 1.
Self-Administered Swab (SAS) Compared to Matched Urine Specimens by LCR: N= 2009



Relative Sensitivity 75.1% (157/209 Positive Predictive Value 87.2% (157/180)

Relative Specificity 98.7% Negative Predictive Value 97.2% (1777/182

POSTER
Sexually Transmitted Diseases
Poster Area Open:
Friday and Saturday, 12:00PM - 2:00PM
Presenters Available:
Friday and Saturday, 12:30PM - 1:30PM

606 Prevalence And Risk Factors Of *C. trachomatis* And *N. gonorrhoeae* Infection In Male Military Recruits

J A Cecil, M R Howell, Johns Hopkins University, Baltimore, MD; J C Gaydos, HM Jackson Foundation, Rockville, MD; K T McKee, Fort Bragg, NC; P Syffus, J L Lindner, Fort Jackson, SC; T C Quinn, Johns Hopkins University; NIH, NIAID, Baltimore, MD; C A Gaydos, Johns Hopkins University, Baltimore, MD

C. trachomatis and *N. gonorrhoeae* urogenital infections are associated with significant morbidity, particularly in women. Because these infections may be asymptomatic, the effectiveness of efforts to limit their impact depends on a thorough understanding of the epidemiology of these infections in both women and men. Male army recruits were tested for *C. trachomatis* and *N.gonorrhoeae* using urine ligase chain reaction to determine the prevalence of these infections. Each volunteer completed a questionnaire providing information on demographic characterisitics, sexual history and symptoms. Among the 2,245 men screened for *C. trachomatis*, the prevalence of infection was 5.3%. Their mean age was 21 years, 60% were Caucasian, and 27% were African-American. Thirty-three percent reported more than one sex partner, 34% had a new sex partner within the previous 90 days and 2.6% reported having had a prior chlamydial infection. Of the men that tested positive for *C. trachomatis*, only 14% reported having symptoms. In multivariate analysis, African-American race (OR 4.4, p<.001), a new sex partner (OR 2.3, p<.001) and the presence of symptoms (OR 4.4, p<.001) were associated with chlamydial infection. Of those screened for *C. trachomatis*, 884 were also tested for *N. gonorrhoeae*. The prevalence of *N. gonorrhoeae* infection was .57%. In this group, 59% were Caucasian, 27% were African-American, 30% reported more than one partner, and 30% reported a new sex partner in the previous 90 days. Additionally, 2.6% reported a prior chlamydial infection and 2.7% reported a history of gonorrhea. Of the men that tested positive for *N. gonorrhoeae*, 40% reported having symptoms and 60% were coinfected with *C. trachomatis*. In multivariate analysis, only a reported history of chlamydia (OR 28.4, p<.002) or a positive test for *C. trachomatis* (OR 35.1, p<.001) were predictive of infection with *N. gonorrhoeae*. Young age was not a predictor of either infection. A substantial number of male army recruits are infected with *C. trachomatis*, but few are infected with *N. gonorrhoeae*. Screening on the basis of symptoms alone would miss the majority of both infections.

607 Clinical Epidemiology Of Trichomonal Vaginitis: Correlates Of Infection Among STD Clinic Attendees

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Background: Vaginal infection with *Trichomonas vaginalis*(TV) is classically associated with vaginal discharge, pruritus, and other clinical findings, and has been shown to be an independent risk factor for HIV acquisition. We evaluated clinical correlates of infection with TV among women attendees of an urban STD clinic. **Methods:** Retrospective chart review of consecutive female patient visits to the St. Louis County STD clinic from 1996-98. Demographic, behavioral, and clinical findings were noted for persons with trichomonal vaginitis by wet mount examination (N=41), gonococcal (GC) or chlamydial (Ct) cervicitis by DNA probe (N=73) and for non-vaginitis/cervicitis patients (N=701). **Results**: Patients with TV were older (p<.001), more likely to have a prior history of trichomoniasis (p=.005), and less likely to have cervical friability, edema, or ectopy on clinical examination (p=.02) than other STD patients. Presence of discharge (55-64%), pruritus (21-32%)and mean duration of discharge (12-19 days) were similar across groups. **Conclusion:** Symptomatic presentation of discharge or pruritus were poor clinical predictors of TV among STD clinic attendees. Older age and prior history of TV correlated strongly with active infection. Greater clinical weight should be placed on these parameters to diagnose incident TV infections in clinical practice.

Clinical Characteristic	TV	GC/Ct	Other	p-value
Age (yrs.)	26.9	21.9	26.4	<.001
Prior hx TV (%)	26.8	6.8	11.6	.005
Abnl. cervix (%)	34.1	57.5	41.5	.02
Pruritus (%)	31.7	21.9	29.4	.37
Discharge (%)	63.4	56.2	55.3	.60
Duration (days)	18.9	16.4	12.4	.12

608 Treatable STD Risk and Prevalence at a Birmingham Substance Abuse Treatment Facility

Laura Bachmann, Ivey Lewis, Ruthie Allen, Jane R Schwebke, Laura Leviton, The University of Alabama at Birmingham, Birmingham, AL; Harvey Siegal, Wright State University School of Medicine, Dayton, OH; Edward W Hook, The University of Alabama at Birmingham, Birmingham, AL

Treatable STD Risk and Prevalence at a Birmingham Substance Abuse Treatment Facility L. H. BACHMANN*[1], I. LEWIS[1], R. ALLEN[1], J. R. SCHWEBKE[1], L. LEVITON[1], H. SIEGAL[2], E. W. HOOK III[1] [1]University of Alabama at Birmingham, Birmingham, AL [2]Wright State University School of Medicine, Dayton, OH Objective: Although strong associations have been reported between drug use and risk for STDs (including HIV), few studies have evaluated STD prevalence in persons entering inpatient drug treatment. We evaluated the prevalence of gonorrhea, chlamydia, trichomoniasis, and syphilis in patients entering inpatient drug treatment. Methods: A questionnaire addressing sexual and substance abuse history was administered and participants submitted urine for chlamydia and gonorrhea LCR testing. Female clients collected a self-obtained vaginal swab for trichomonas culture. Phlebotomy for VDRL and voluntary HIV testing was performed. Results: Two hundred and fifty patients, 164 (66%) males and 86 (34%) females, were enrolled; 64% were African-American and the mean age was 35 (18 65). Crack use was reported by 68% of participants and 72% reported polysubstance use. STD risk behaviors were common: 47% reported multiple sex partners during the previous 6 months and 14% one or more new sex partners in the past 30 days. Exchange of sex for drugs or money was reported by 40% of women and 15% of male participants. Chlamydia prevalence was 2.8% in clients under 30 years of age and 1.1% in those older than 30. Gonorrhea prevalence was uniform across both age groups (1.4% and 1.7%, respectively). Six percent of clients with VDRL results available (N=240) were reactive and 44% of women had a positive trichomonas culture. Conclusions: Trichomoniasis was extremely common in the female members of the population. Despite a high prevalence of STD risk behaviors, the lower than anticipated prevalence of gonorrhea and chlamydia may be related to the older age of patients at this treatment facility. Nonetheless, STD risk reduction counseling and screening may be a useful adjunct to inpatient drug treatment.

609 Fitz-Hugh-Curtis-Like Syndrome Caused By Herpes Simplex Virus

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Fitz-Hugh-Curtis syndrome is perihepatitis associated with *N. gonorrhoeae* or *C.trachomatis* infection. We present a patient who presented with Fitz-Hugh-Curtis-like syndrome caused by Herpes simplex virus. A 28 y/o Filipino woman, gravida 0, para 0, was admitted for abdominal pain and fever. Her LMP was 10 days PTA. She had had varicella and Herpes labialis, but no Herpes genitalis. 5 days PTA she had hives after eating eggs. She had finished a tapering course of prednisone on the day of admission. 3 days PTA, she developed high fever, abdominal pain, a yellow vaginal discharge, and dysuria. She had one stable sexual partner. Her temperature was 39^{0}C and BP 99/53 mm Hg. Abdomen was tender, lower > upper quadrants. Pelvic examination showed Herpes genitalis on the labia majora, yellow cervical discharge, and cervical motion tenderness. White count was 10,400 cells/μL, 85.5% N, 10% L, 3.6% M, 0.1% E, and 0.8% B. Pelvic USG showed a small amount of fluid. She was given cefotetan 2 gram i.v. q 12 h, and doxycycline 100 mg i.v. q 12 h. Fever persisted. DNA probes for gonococci and Chlamydia were negative. Abdominal CT showed pelvic fluid. Laparoscopy showed erythema of the uterus and the fallopian tubes and serosanguinous fluid in the cul-de-sac. The liver showed multiple vesicular lesions 0.2 to 0.5 cm in diameter. Biopsies showed acute herpetic hepatitis and foci of hepatocellular necrosis. Immunostains for herpes antigen were positive. The serosanguinous fluid grew Herpes simplex virus. Liver function tests showed AST 6219 U/L (nl=14-36), ALT 4673 U/L (9-52), alkaline phosphatase 188 U/L (38-126), total bilirubin 1.7 mg/dl (0.2-1.3). HBsAg, HepCAb and HIV tests were negative. Acyclovir 500 mg iv q 8 h and ampicillin/sulbactam 3 gm iv q 8 h were started. Cefotetan and doxycycline were discontinued. She became afebrile on day 6. On day 8, acyclovir and ampicillin/sulbactam were discontinued. Famciclovir 1 gm p.o. q 8 h and amoxicillin/clavulanate 500 mg p.o. q 8 h were started. She was discharged home on day 10. Four months later she is doing well. Thus, our patient presented with Fitz-Hugh-Curtis-like syndrome associated with Herpes simplex virus. To our knowledge, this is the first report of this entity.

610 Outbreaks Of Syphilis At Three Men's State Prisons, Alabama, 1998-1999

Mitchell I Wolfe, Fujie Xu, Priti Patel, Centers for Disease Control and Prevention, Atlanta, GA; Michael O'Cain, Alabama Department of Public Health, Montgomery, AL; Julia A Schillinger, Michael E St Louis, Lyn Finelli, Centers for Disease Control and Prevention, Atlanta, GA

Background: Syphilis is an acute and chronic sexually transmitted disease that enhances HIV transmission. In February 1999, outbreaks of syphilis were reported at three Alabama State men's prisons. Men are screened for syphilis when entering prison; subsequent syphilis infection is likely prison-acquired. We investigated potential methods of syphilis introduction into and dissemination within the prison system, and missed opportunities for syphilis control. **Methods:** We reviewed medical records, patient interview records and transfer records. **Results:** At three prisons from April 1998 - February 1999, 39 cases of early syphilis were identified among approximately 2,500 men (27, 5, and 7 cases at Prisons A, B, and C, respectively), a tenfold increase over baseline. Prison C houses HIV-infected men. The annualized incidence rate for early syphilis was 1337/100,000 in these prisons. Case-patients identified a median of two sex partners (range 0-18) and many concurrent sexual partnerships within the infectious period; 31/38 (82%) identified a partner with early syphilis. Outbreaks at Prisons A and B were epidemiologically linked. No index case was identified; however, four case-patients were incarcerated in local jails, and six were resident in another prison, during the likely time of syphilis exposure. At Prison A, an early outbreak case was 11 times more likely to have been exposed to jail or transferred from another prison than a later outbreak case [OR=11.2, 95% CI=1.2-139.7, p=0.02). Medical record review demonstrated delays in syphilis testing/treatment for persons with signs of syphilis. **Conclusions:** Likely sources of syphilis introduction included sexual mixing of prisoners with unscreened jail populations, and transfer of infected prisoners between facilities, while dissemination of syphilis was facilitated by delayed treatment, and multiple, concurrent sexual partnerships. Recommendations include mass syphilis screening of prisoners during outbreaks, syphilis screening annually and upon return from jails, training medical staff in diagnosis and treatment, and sexual risk reduction counseling, including condom availability.

Prevalence by urine ligase chain reaction and risk factors for *Chlamydia trachomatis* in a large cohort of military women over four years

CA Gaydos[1], MR Howell[1], TC Quinn[1,2], M Theodore[1], P Syffus[3], J Lindner[3], KT McKee, Jr[4], JC Gaydos[5]

[1]Johns Hopkins University, Baltimore, MD, [2]NIAID, NIH, Bethesda, MD, [3]Ft. Jackson, SC, [4]Ft. Detrick, MD, [5]DoD Global Emerging Infections Surveillance & Response System, Washington, DC.

Introduction

At present, there is no routine screening program for chlamydia in the U.S. Army. A large cohort of non-health care seeking female Army recruits was enrolled in a chlamydia screening program over 4 years in order to assess prevalence and STD risk factors, as well as any temporal changes in prevalence and risk factors.

Methods

Recruits (N=23,010) at Ft. Jackson, SC, provided informed consent and were enrolled for study. Urine was tested by ligase chain reaction and questionnaires were used to collect demographic and sexual risk data. Regional changes in prevalence were examined. Data analysis was by Intercooled Stata 4.0.

Results

The mean age was 20.6 yr (range 16-39). The volunteer rate was 79%; and 50.5% were Caucasian, 35.6% were African American, and 13.9% were other races. Prevalence for all years was 9.5%; for Year 1996: 441/5,185 (8.51%); Year 1997: 779/8,047 (9.68%); Year 1998: 510/5,150 (9.90%); and Year 1999: 459/4,628 (9.92%) ($p = 0.018$). State home of record was also a determinant of risk for infection. Using 1996 as the referent, prevalences for other years were significantly higher. Analysis of trends in behavior revealed a decrease in risk over 4 years for having > 1 sex partner and a new sex partner ($p < 0.00$), but condom use was unchanged ($p = 0.24$). Overall, 90.7% reported vaginal sex, but fewer reported vaginal sex in years 1997-99 (92-82%) using 1996 (93.75%) as the referent (p=0.00-0.01). Over the 4 years, the mean age changed from 21.0 years in 1996 to 20.4 in 1997, 20.6 in 1998 and 20.3 in 1999. By regression analysis, the decrease in age was significant. The proportion of the population <25 years increased from 84.5% in 1996 to 87.3%, 84.5%, and 86.1% for years 1997-99, respectively.

Conclusions

Reductions in sexual risk behavior are encouraging. The use of the proportion of those <25 years of age as a variable in the model appeared to account for the increase in prevalence over time. Young age remains a consistent determinant of risk for chlamydia infection and screening is recommended for young female military recruits.

CHANGES IN PREVALENCE AND RISK FACTORS OVER FOUR YEARS IN A URINE BASED CHLAMYDIA SCREENING PROGRAM FOR FEMALE ARMY RECRUITS

Gaydos, CA, DrPH; Howell, MR, MS; Johns Hopkins University, Baltimore, MD: Quinn, TC, MD, NIAID, NIH, Bethesda, MD: McKee,Jr, KT MD, Ft. Detrick, MD: Gaydos, JC, MD, DoD Global Emerging Infections Surveillance Response System, Washington, DC.

A cohort of 23,010 non-health care seeking female Army recruits were enrolled in a chlamydia screening program over 4 years in order to assess changes in prevalence and STD risk factors. Urine was tested by ligase chain reaction and questionnaires were used to collect demographic and risk data. Data analysis was by Intercooled Stata. Prevalence for all years was 9.5%; for Year 1996:441/5185 (8.51%); Year 1997: 779/8047 (9.68%); Year 1998: 510/5150 (9.90%); Year 1999: 459/4628 (9.92%) (p 0.018). Using 1996 as the referent, prevalences of other years were significantly different. Risk factors analysis revealed: > 1 sex partner ranged from 24.01% for year 4 to 27.28% for year 2 (p 0.00); new sex partner ranged from 26.88% in year 4 to 32.5% in year 2 (p 0.00); condom use ranged from 15.27% for year 1 to 16.52% for year 3 (p 0.244). Overall, 90.7% reported vaginal sex, but fewer reported vaginal sex in years 1997-99 (92-82%) using 1996 (93.75%) as the referent (p=0.00-0.01). Over the 4 years, the mean age changed from 21.02 years in 1996 to 20.39 in 1997, 20.62 in 1998 and 20.32 in 1999. By regression, the decrease in age was significant. The proportion of the population <25 years increased from 84.51% in 1996 to 87.28%, 84.54%, and 86.08% for years 1997-99. Reductions in risk are encouraging. The <25 years age group as a variable in the model accounted for the increase in prevalence over time. Age remains a consistent determinant of risk for chlamydia infection.

Collection of a Self-Administered Swabs versus Urine for Diagnosis of *C. trachomatis* by DNA Amplification: Insight Into Patient Preferences

MR Howell[1], J Gaydos[2], KT McKee, Jr.[3], TC Quinn[1,4], CA Gaydos[1]
[1]The Johns Hopkins Univ, School of Medicine, Div. of Infectious Diseases, Baltimore, MD; [2]DoD Global Emerging Infection Surveillance & Response Sys., Washington, DC; [3] Fort. Detrick, MD [4]NIAID, NIH, Bethesda, MD

Introduction

Use of self-administered swabs (SAS) for the detection of *C. trachomatis* by DNA amplification simplifies specimen collection and transport. SAS may be a useful adjunct to medical care for military and other women in field or non-clinical settings. Both urine and SAS have been shown to be sensitive for the detection of chlamydia. As part of an evaluation of SAS, we assessed female preferences for collection of SAS versus urine.

Methods

4,496 female Army recruits entering basic training at Ft. Jackson, NC from 3/99 to 8/99 were invited to participate. All participants provided urine and a self-administered swab, and completed a preference questionnaire. Associations with participant characteristics were assessed using logistic regression (Intercooled STATA 4.0). Comparisons with p-values<.01 are reported. To assess actual selection of collection method, women were offered a choice of either urine or a SAS on two collection dates.

Results

31% (1,403/4,496) of women completed questionnaires and provided both specimens. A chlamydia positivity rate (by either method) of 11.8% (166/1,403) was observed. Overall, 90.5% (1,270/1,403) said they felt comfortable collecting the urine specimen; while, only 69% (968/1403) said they felt comfortable collecting SAS. At home, 90.8% (1,274/1,403) of respondents said that they would prefer to collect a urine specimen if they thought they were at risk for infection and 82.8% (1,161/1,403) would collect a SAS. In the field, 79.4% (1,114/1,403) women said they would prefer collecting urine, and 68.8% (965/1,403) SAS. When questioned on ease of use, 60.5% said urine was the easier method. When given a choice (urine or SAS) 63.2% (791/1,251) would collect urine in a clinic setting; 57.4%(733/1,276) in a home setting; and 58.1% (706/1,216) in a field setting. In general, women reporting sexual risk behavior (more than 1 sex partner and/or new sex partner and/or no condom) and women reporting white race were more likely to be comfortable with the SAS method. Women reporting risk were more likely to indicate that they would prefer to collect a SAS in the clinic, home, and field settings. Women reporting white race were more likely to indicate that they would prefer to collect a SAS in a field setting. These differences did not vary by age. However, younger individuals and those reporting black race more frequently reported discomfort catching the urine in the cup. Individuals not reporting risk and those reporting a race other than white more frequently reported discomfort collecting and carrying SAS. Older individuals more frequently reported pain associated with collection of SAS. Later in the study, when women were given an active choice to provide either SAS or a urine specimen, 93% (388/417) actually provided urine.

Discussion

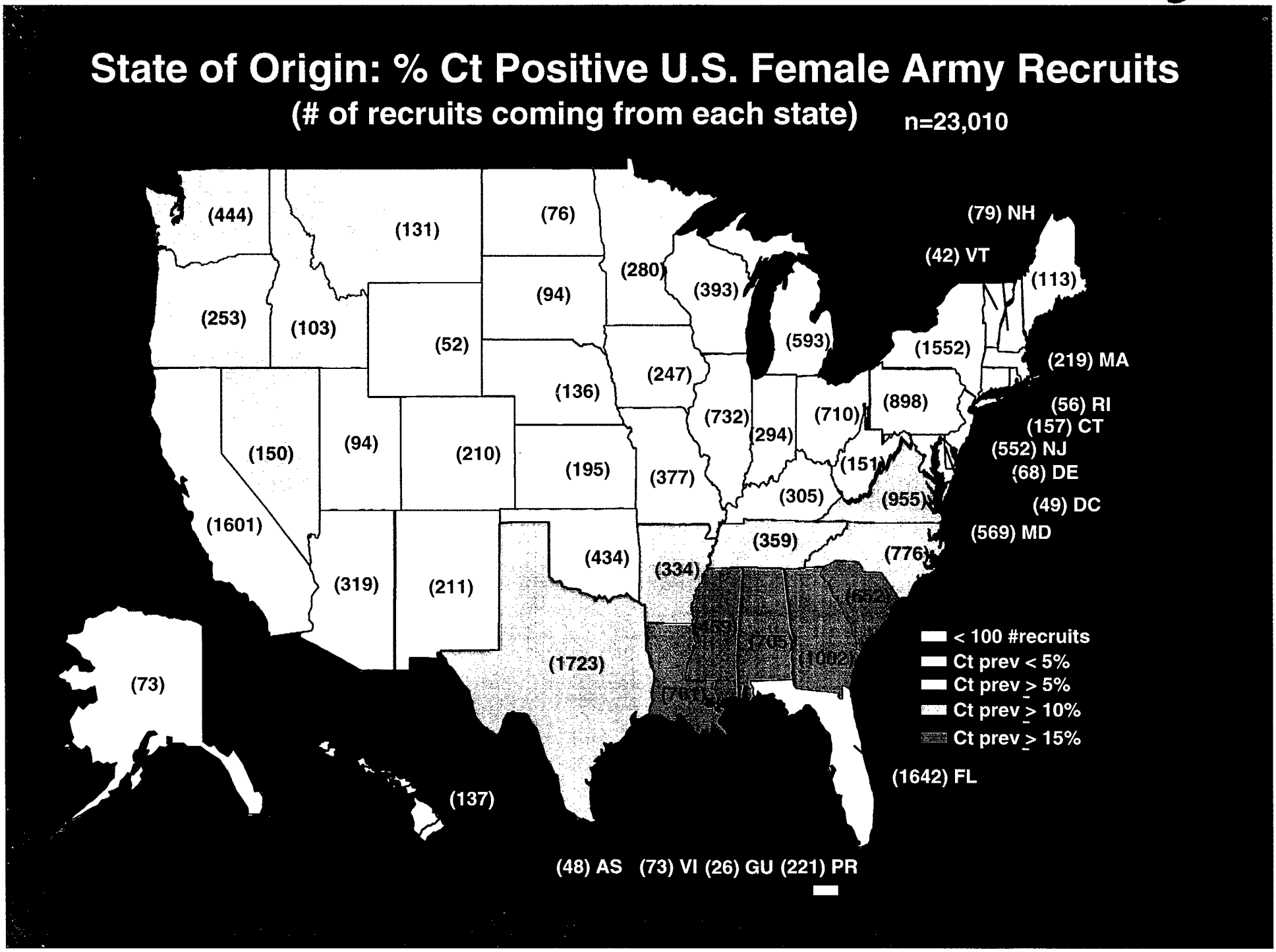
Women indicating sexual risk taking were more comfortable using SAS, while those reporting no risk and race other than white preferred urine. When given a choice, the women exhibited a strong preference for urine. However, many would use SAS if offered and felt relatively comfortable using the SAS. These results indicate potential acceptability in settings not amenable to cervical or urine collection, however, this requires field testing.

11.3 Maps

Percentage Chlamydia Positive Females by Geographic Origin for Project Years 1-4

State of Origin: % Ct Positive U.S. Female Army Recruits

(# of recruits coming from each state) n=23,010



11.4 Armed Forces Epidemiology Board and the Institutional Review Boards of Johns Hopkins University and Ft. Jackson (Eisenhower, Ft. Gordon)

the patient was hospitalized. The patient was found to have complete heart block, systolic BP over 200mmhg, potassium level of 7.9mg/dl. She was dialyzed and a pacemaker was placed. The patient became stableand pacemaker was removed. The reporting physician felt that hyperkalemia was related to therapy with Losartan or control. The report dated 26 Jan 98 involved a 68 year old male patient who had ahistoryof asthma and was hospitalized for asthma. The patient recovered and was discharged from the hospital. The reporter felt that the asthma was possibly related tos tudy drug therapy. Four patients have been enrolled in this study at EAMC. There has been an adverse event at this site for ruled-out MI.

Recommendation: Full Committee Acknowledges

The Informed Consent dated 11 Sep 97 was submitted to delete the following statement, "If you are male, you should avoid fathering children by using condoms when having sexual intercourse unless you have had a vasectomy". The legal department of Merck, Inc requested the removal of this statement.

Recommendation: Approve

Human Use Committee Vote: 10 in favor, unanimous

5. Protocol Review:

Study of Chlamydia Trachomatis in Military Women: Prevalence, Risk Factors and a Cost Benefit Analysis of Early Diagnosis and Treatment
PI: LTC Rose M. Hendrix, MC
DDEAMC 95-17

With regard to Minutes of the Institutional Review Committee Meeting 12 March 1998, the investigator offered the following replies to questions raised by the committee: We propose that not only will the mass therapy option cure chlamydia, but a significant proportion of the additional cases of gonorrhea, and respiratory infections as supported above. The cost of hospitalized pelvic inflammatoary disease and ectopic pregnancy are staggering for the military. The prevention of these sequelae diseases and their associated costs is the focus of this proposal. The results of a cost effective decision model we have performed has indicated that the most cost-effective strategy for the Army would be mass therapy, mostly because the diagnostic test is not perfect and the extra infections cured and sequelae prevented offset the extra cost of antibiotic. Anecdotal data from the current study has indicated that in over 1,000 women treated with single-dose azithromycin, there has only been one adverse event that caused a recruit to seek medical attention. It was not classified as serious. Further, a tabulation of 6 studies published from 1992-1998 substantiates a lack of significant differences for serious adverse episodes between individuals treated with azithromycin therapy compared to those receiving doxycycline. Reactions were considered mild to moderate and were noted primarily to be gastrointestinal in nature (diarrhea, nausea, etc). Additionally, use of mass therapy with azithromycin in a large trial (12,000 volunteers; 6,000 each of treatment arm and control arm) in Uganda has not reported any serious adverse events. The 6,000 volunteers have been treated four times. Confusion relating to misclassification of azithromycin as a macrolide (e.g., erythromycin) is frequent. The issue of pregnancy should be of no impact upon this protocol. Upon in-processing at Ft. Jackson, recruits are screened for possible pregnancy and pregnant women are not allowed to continue in basic training (EPTS). Azithromycin is a class B drug and is currently being given in clinical practice to pregnant patients. A modification of the consent form has been appended to clarify that there are no benefits to participating in this study for an individual who has never engaged in sexual activity

MCHF-CI 9 April 1998
SUBJECT: Minutes of the Institutional Review Committee Meeting 9 April 1998

It is well known in behavior research that there exists a high probability for a respondent to misrepresent herself. In this study we have documented 14 chlamydia infections in females who had denied sexual activity. Additionally, in analyzing demographic information on individuals choosing to not participate, it is clear the only significant difference between that group and those participating is in engagement in sexual activity. Any woman engaging in even a single episode of unprotected sexual activity in the past, can be at risk for asymptomatic disease or its sequelae. Although evidence is accumulating that there are no serious drug interactions, the investigators will ask recruits to list medications they are taking if they participate. This information will be carefully studied and tabulated. They think the consent form, which is the routine Army consent form DA Form 5303-R is clear on this point. However, they will instruct the civilian study nurse to reiterate that participation is entirely voluntary. The study nurse reports that when recruits talk to her afterwards they express concern to know whether they are infected since most chlamydial infections are asymptomatic in women. PID, ectopic pregnancy, and infertility are valid concerns of these women. They consider that the high volunteer rate is a reflection of the nurses' excellent teaching skills regarding the potential serious sequelae. (Probability of developing PID after chlamydial infection is 30% Howell et al). The recruits' desire to know about their health pales in comparisons to the ease of the collection of urine specimen.

The committee reviewed the submitted responses to its questions from the 12 March 98 meeting. Azithromycin is, in fact, an azalide antibiotic which is a subclass of macrolides structurally, but possess a very different milder side effects profile.The principal argument in favor seems to be an economic one. Based on the assumptions of the model, fewer cases of PID or asymptomatic chlamydia would result. The assumptions were challenged that a single dose could have such lasting effects. The training dollars lost could probably not be detailed that precisely. True, EPTS discharges occur but often for undiagnosed abdominal pain and not proven PID. Some are for endometriosis and other menstrually related dysmenorrhea. Silent chlamydia would show largely during an infertility workup. The need for recycling in training as a result of PID seemed high to members who have been or are currently involved in AIT and basic training. The basis for some of those lost training dollars was questioned.

The principal reason for doing the study would be for a potential policy for future basic trainees. If women (or men) were forced to take an antibiotic and developed a severe side effect, they might have a basis for a future claim against the government despite the current rule against suit by active duty members. The trend in medicine in antibiotic usage is against most prophylactic use except in very limited settings of respiratory or unavoidable threat. Otherwise disease is tested for and then treated, especially when a relatively good test is available. It is only for the false negatives that an issue exists. Repeat testing at a later date might pick up some of these false negatives, but this is not part of the study design. The issue of emerging resistance patterns was also cited. Several committee members expressed the feeling that they would be personally offended at being expected to take a pill to treat a presumed STD. The ethical issues for humans is different than that of a swine herd. The Army does not require mass prophylaxis unless the environmental threat is unavoidable. The clinical standard is still to test and then treat.

The original protocol was an all female study, however, it would be useful to know how the prevalence of chlamydia in the female recruit population compares to that of males in the same population. What they have proposed is that they test approximately 1000 male volunteers following the current protocol. These males would be counseled and tested in single gender groups by the same non-military protocol nurse we are presently using for the females. Those individuals testing positive would be referred for treatment, as are the females currently. Once male volunteers have been tested, they would go back to the original protocol and test only females for the remainder of the study.

ray-6

MCHF-CI 9 April 1998
SUBJECT: Minutes of the Institutional Review Committee Meeting 9 April 1998

Recommendation: Approve the male prevalence testing arm and correct minor errors in consent form

Clinical Investigation Committee Vote: 10 in favor, unanimous

Human Use Committee Vote: 10 in favor, unanimous

Recommendation: Disapprove the mass treatment arm.

Clinical Investigation Committee Vote: 10 in favor, unanimous

Human Use Committee Vote: 10 in favor, unanimous

6. Amendments:

A Randomized, Double-Blind, Multicenter comparison to the Efficacy and Safety of Grepafloxacin (Raxar) 400mg or 600mg Once Daily and Clarithromycin (Biaxin) 500mg Twice Daily in the Treatment of Patients with Acute Bacterial Exacerbations of Chronic Bronchitis
PI: LTC Warren L. Whitlock, MC
DDEAMC 98-17

A letter from Pharmaceutical Research Associated, Inc dated 3 Mar 98 was received regarding an amendment to this study. This amendment changes from patients with known moderate or severe hepatic or renal disease to hepatic failure or known moderate to severe renal disease. It also changes the primary efficacy population from patients who are clinically evaluable to clinically and bacteriologically evaluable. And therefore, changing the secondary efficacy population from bacteriologically evaluable to clinically evaluable. The third change in the amendment changes the package inserts for Biaxin and Raxar.

Recommendation: Approve
Human Use Committee Vote: 10 in favor, unanimous

7. Periodic Review:

A Randomized, Multicenter, Third Party Blinded Trial Comparing Trovafloxacin with Amoxicillin/Clavulanate (Augmentin) with or without Erythromycin for the Treatment of Community Acquired Pneumonia
PI: LTC Warren L. Whitlock, MC
DDEAMC 97-26

There has been good response to treatments with this drug. Trovafloxacin has now been approved by the FDA to treat Community Acquired Pneumonia and we have been part of that. A total of 16 patients have been enrolled and only one serious adverse event has been reported.

Recommendation: Approve
Human Use Committee Vote: 10 in favor, unanimous

11.5 Quarterly Reports

Rene Howell
11/8/99

C. trachomatis Screening: U.S. Army Female Recruits

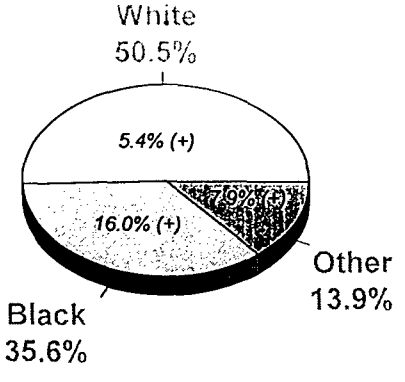
(1/21/96 through 9/30/99)
Female N=23,010
Male N=2,278

Female *C. trachomatis* prevalence = 9.51% (2,189/23,010)
urine: 9.4% (2,142/22,698)
swab: 8.8% (2,04/2,321)

Male *C. trachomatis* prevalence = 5.2% (118/2,278)

Demographics, all women:

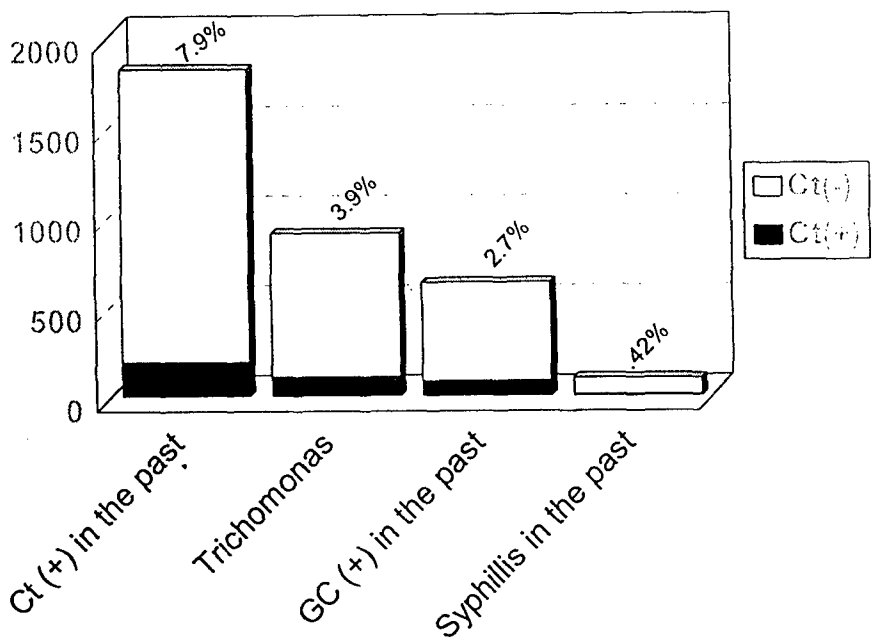
Mean age = 20.6 ± 3.63
range (16 - 39



Behavioral Risk Factors, all women:

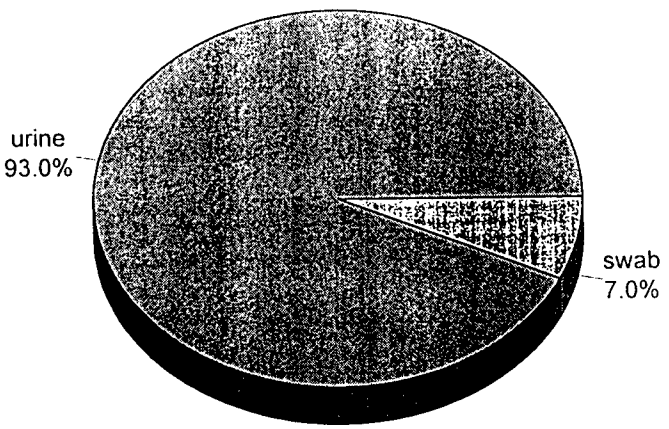
	No. Of Women (%)		LCR Positive, %
Vaginal Intercourse			
yes	20,883	(90.8)	10.2%
no	2,079	(9.0)	2.6%
missing	48	(.2)	0.1%
More than 1 sex partner, last 90 days			
yes	5,973	(26.0)	14.0%
no	16,580	(72.0)	8.1%
unknown/missing	457	(2.0)	3.7%
New sex partner, last 90 days			
yes	6,815	(29.6)	12.6%
no	15,645	(68.0)	8.3%
unknown/missing	550	(2.4)	5.8%
Consistent condom use, last 90 days			
yes	3,710	(16.1)	9.0%
no	17,996	(78.7)	10.0%

unknown/missing	1,304	(5.7)	3.7%
Symptoms			
yes	4,069	(17.7)	12.5%
no	17,748	(77.1)	8.9%
unknown/missing	1,193	(5.2)	8.7%



20,136 (87.5%) women did not have a previous STD. 1,375 (9.3%) of these women we Ct (+).

Rene Howell
11/8/99



Rene Howell
8/5/99

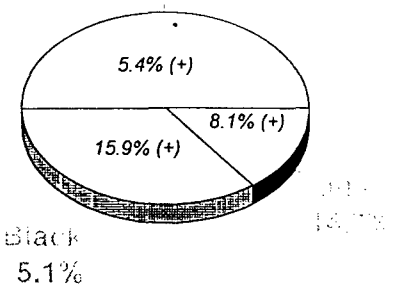
Army Data

(1/21/96 through 6/30/99)
Female N=21,872
Male N=2,278

Female *C. trachomatis* prevalence = 9.48% (2,247/21,872)
urine: 9.5% (2,044/21,568)
swab: 9.0% (127/1,407)

Male *C. trachomatis* prevalence = 5.2% (118/2,278)

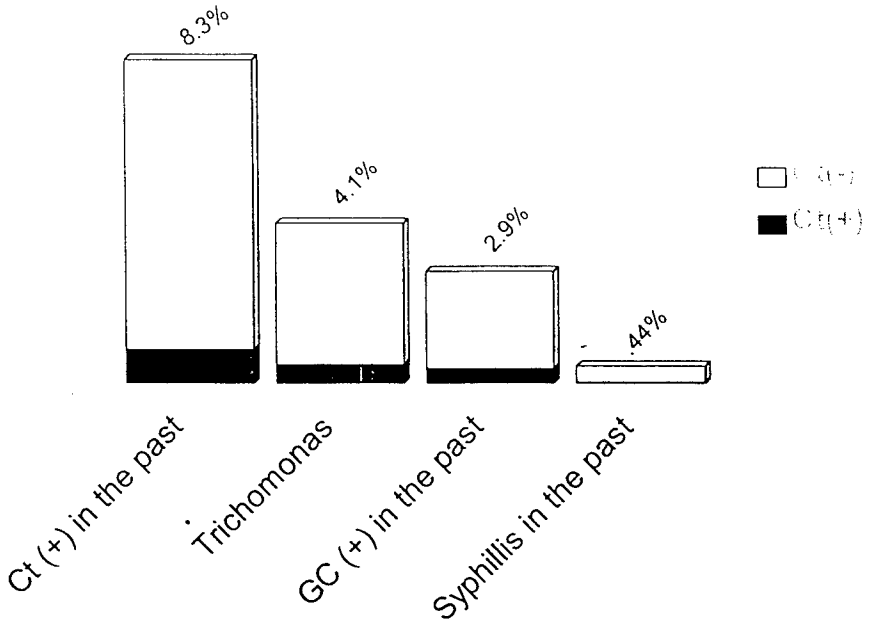
Demographics, all women:



Behavioral Risk Factors, all women:

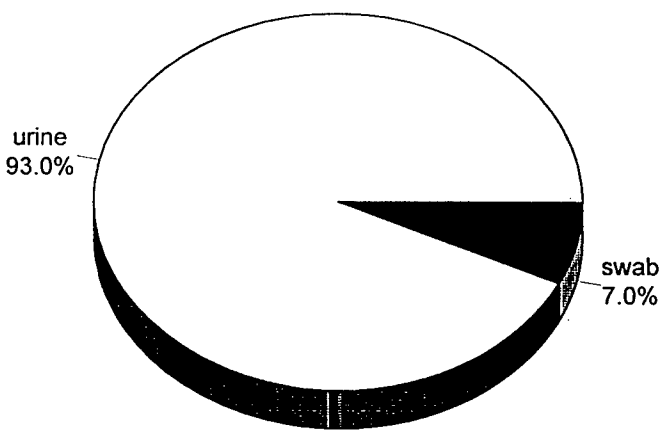
	No. Of Women (%)		LCR Positive, %
Vaginal Intercourse			
yes	19,964	(91.3)	10.1%
no	1,861	(8.5)	2.6%
missing	47	(.2)	4.3%
More than 1 sex partner, last 90 days			
yes	5,691	(26.0)	13.9%
no	15,852	(72.5)	8.0%
unknown/missing	329	(1.5)	3.7%
New sex partner, last 90 days			
yes	6,508	(29.8)	12.5%
no	14,947	(68.3)	8.3%
unknown/missing	417	(1.9)	6.2%
Consistent condom use, last 90 days			
yes	3,525	(16.1)	8.9%
no	17,225	(78.8)	9.9%
unknown/missing	1,122	(5.1)	3.8%
Symptoms			

yes	3,933	(18.0)	12.6%
no	16,781	(76.7)	8.8%
unknown missing	1,158	(5.3)	8.8%

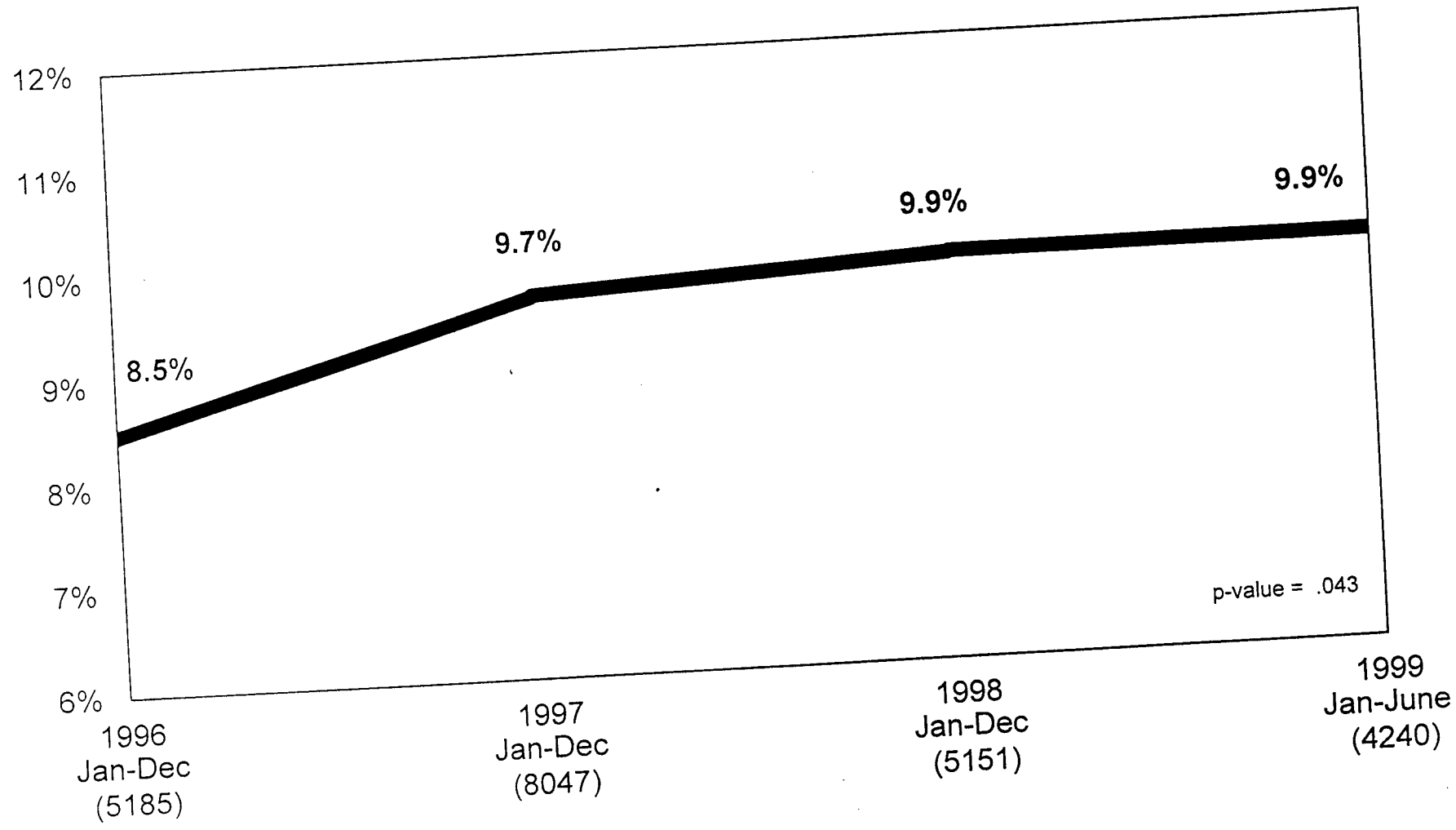


[illegible] Ct (+).

Specimen Collection Preferences
n = 413



Annual Trends in Point Chlamydia Prevalence:
January 1996 - June 1999



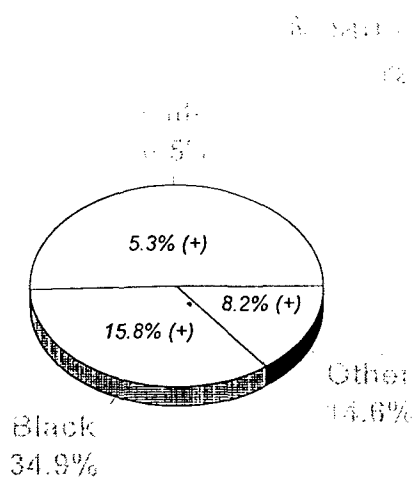
Rene Howell
4/9/99

Army Data

(1/21/96 through 3/31/99)
Female N=19,921
Male N=2,166

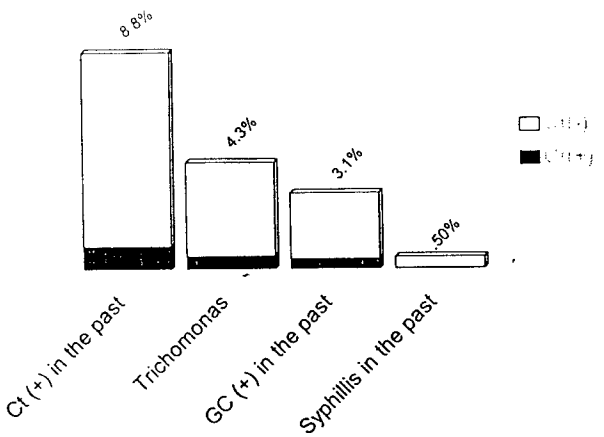
Female *C. trachomatis* prevalence = 9.4% (1,727/18,360)
Male *C. trachomatis* prevalence = 5.2% (118/2,166)

Demographics, all women:



Behavioral Risk Factors, all women:

	No. Of Women (%)		LCR Positive, %
Vaginal Intercourse			
yes	18,375	(92.2)	10.0%
no	1,511	(7.6)	2.5%
missing	35	(0.2)	5.7%
More than 1 sex partner, last 90 days			
yes	5,257	(26.4)	13.7%
no	14,423	(72.4)	7.9%
unknown/missing	241	(1.2)	3.7%
New sex partner, last 90 days			
yes	5,985	(30.1)	12.4%
no	13,607	(68.5)	8.2%
unknown/missing	264	(1.9)	6.1%
Consistent condom use, last 90 days			
yes	3,161	(15.9)	8.7%
no	15,765	(79.1)	9.9%
unknown/missing	995	(5.0)	4.0%
Symptoms			
yes	3,705	(18.6)	12.4%
no	15,199	(76.3)	8.7%
unknown/missing	1,107	(5.1)	8.8%


8.8%
4.3%
3.1%
.50%
Ct (+) in the past
Trichomonas
GC (+) in the past
Syphillis in the past

Rene Howell
1/26/99

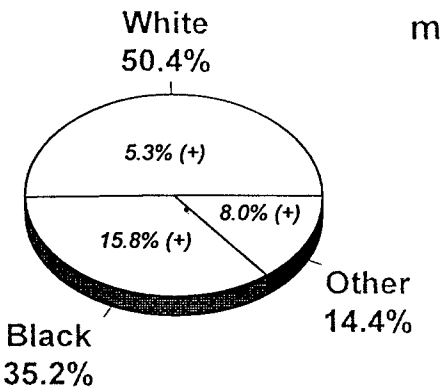
Army Data

(1/21/96 through 12/31/98)
Female N=18,360
Male N = 1,457

Female *C. trachomatis* prevalence = 9.4% (1,727/18,360)
Male *C. trachomatis* prevalence = 5.7% (83/1,457)

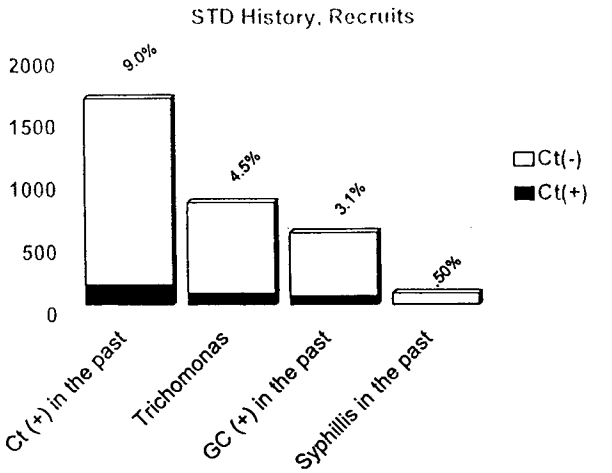
Demographics, all women:

Mean age = 21.1 ± 3.63
range (17 - 39)
missing 99

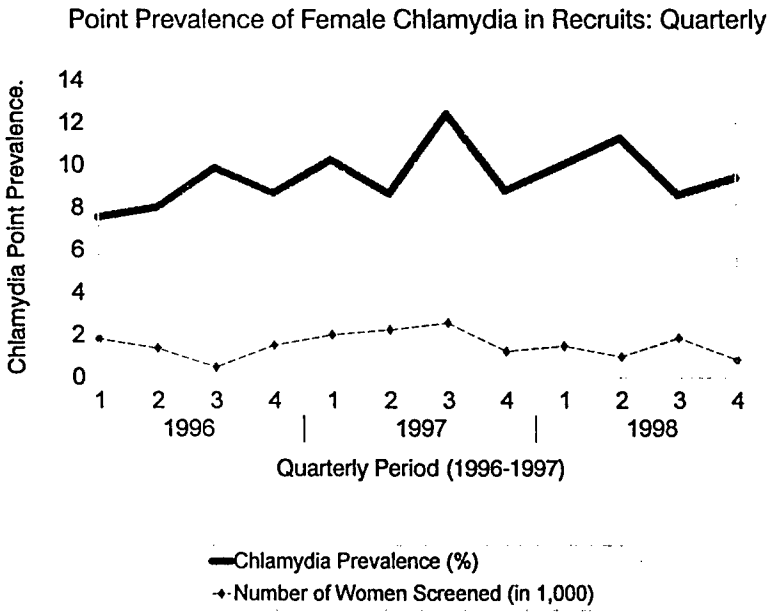


Behavioral Risk Factors, all women:

	No. Of Women (%)		LCR Positive, %
Vaginal Intercourse			
yes	17014	(92.7)	10.0%
no	1299	(7.1)	1.3%
missing	47	(.3)	12.8%
More than 1 sex partner, last 90 days			
yes	4860	(26.5)	13.7%
no	13275	(72.3)	7.9%
unknown/missing	225	(1.2)	4.0%
New sex partner, last 90 days			
yes	5570	(30.3)	12.5%
no	12489	(68.0)	8.1%
unknown/missing	301	(1.6)	5.3%
Consistent condom use, last 90 days			
yes	2963	(16.1)	8.8%
no	14451	(78.7)	9.9%
unknown/missing	946	(5.2)	3.7%
Symptoms			
yes	3441	(18.7)	12.4%
no	13897	(75.7)	8.7%
unknown/missing	1022	(5.6)	8.6%



10,868 (86.4%) women did not have a previous STD. 1,463 (9.2%) of these women were Ct (+)



Rene Howell
10/16/98

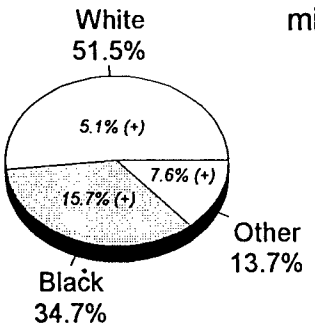
Army Data

(1/21/96 through 9/30/98)
N=18,844

C. trachomatis prevalence = 9.12% (1,719/18,844)
C. trachomatis prevalence 1998 = 8.9% (499/5,614)

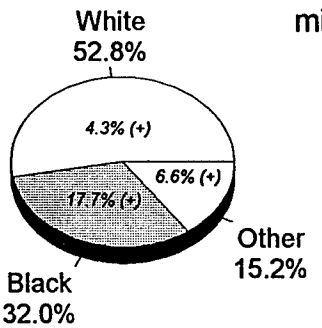
Demographics, all women:

Mean age = 21.0 ± 3.57
range (17 - 39)
missing 103



Demographics, 1998:

Mean age = 20.8 ± 3.5
range (17 - 39)
missing 118



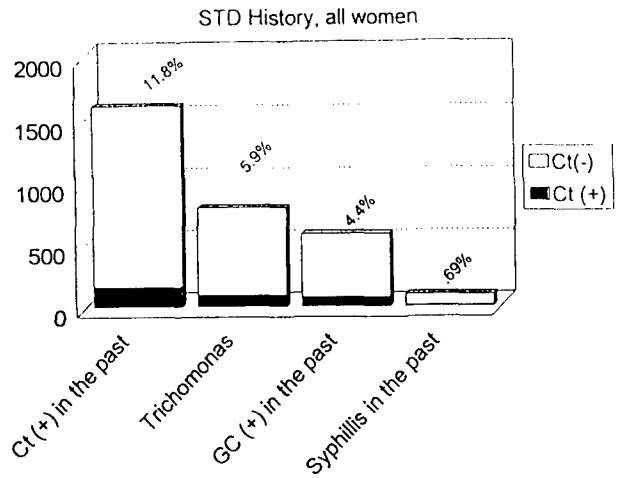
Behavioral Risk Factors, all women:

	No. Of Women (%)	LCR Positive, %
Vaginal Intercourse		
yes	17,369 (92.4)	9.78%
no	1,430 (7.6)	1.12%
missing	9 (.05)	11.11%
Symptoms		
yes	3,417 (18.5)	12.47%
no	14,688 (79.5)	8.39%
missing	368 (2.0)	5.98%
More than 1 sex partner, last 90 days		
yes	5,056 (26.9)	13.33%
no	13,544 (72.0)	7.65%

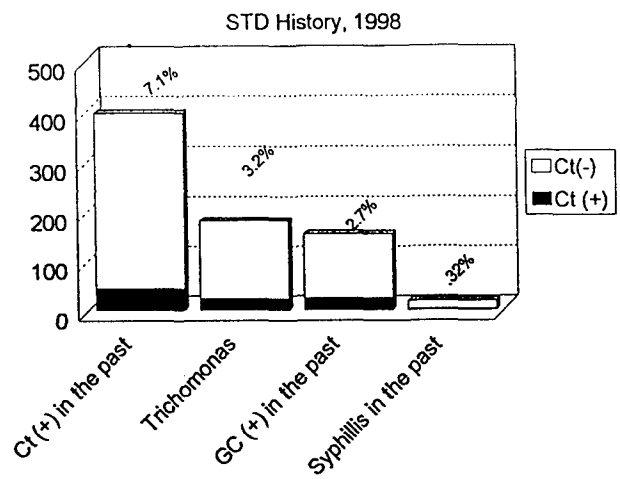
unknow/missing	203 (1.1)	4.43%
New sex partner, last 90 days		
yes	5,799 (30.8)	12.14%
no	12,730 (67.7)	7.86%
unknown/missing	273 (1.5)	5.49%
Consistent condom use, last 90 days		
yes	3,086 (16.5)	8.43%
no	14,747 (79.1)	9.65%
unknown/missing	322 (1.7)	10.56%

Behavioral Risk Factors, 1998:

	No. Of Women (%)	LCR Positive, %
Vaginal Intercourse		
yes	5,063 (90.8)	9.72%
no	515 (9.2)	.58%
missing	0 (0)	0.0%
Symptoms		
yes	933 (17.8)	13.29%
no	4,308 (82.2)	7.82%
missing	3 (06)	0.0%
More than 1 sex partner, last 90 days		
yes	1,567 (28.1)	12.95%
no	3,971 (71.2)	7.43%
unknow/missing	37 (0.66)	2.70%
New sex partner, last 90 days		
yes	1,713 (30.7)	11.56%
no	3,811 (68.4)	7.85%
unknown/missing	48 (0.86)	4.17%
Consistent condom use, last 90 days		
yes	968 (17.9)	8.57%
no	4,319 (79.6)	9.38%
unknown/missing	136 (2.5)	6.7%



16,402 (89.9%) women did not have a previous STD. 1,456 (8.9%) of these women were Ct (+).



5,010 (89.2%) women did not have a previous STD. 427 (8.5%) of these women were Ct (+).

Rene Howell
7/7/98

Army Data

(1/98 through 6/98)

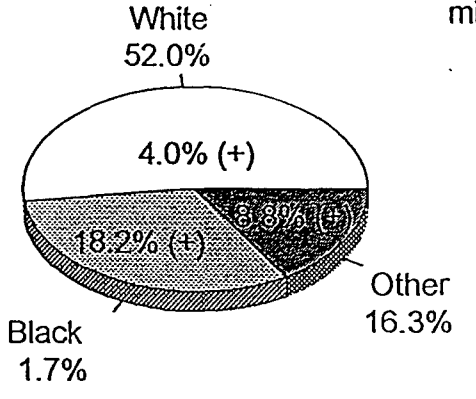
N=3,650
Women = 2,447 Men = 1,203

C. trachomatis prevalence = 7.8% (286/3650)

Women = 9.3 % (227/2447) Men = 4.9% (59/1203)

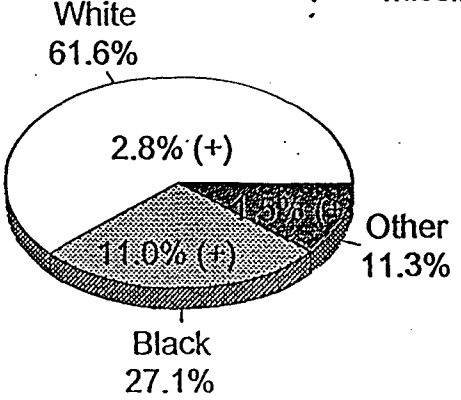
Demographics, all women:

Mean age = 21.7 + 3.81
range (17 - 36)
missing 26



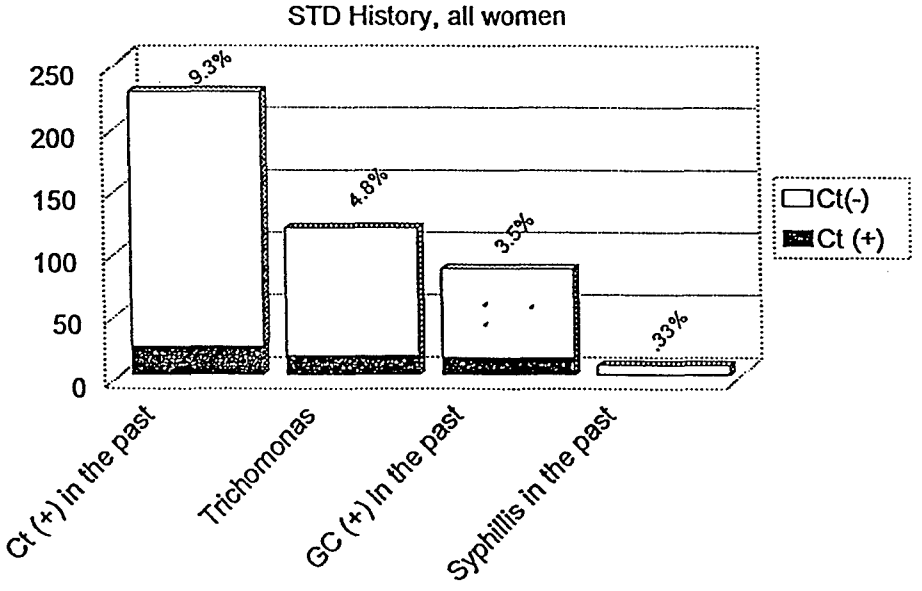
Demographics, all men:

Mean age = 19.8 + 2.61
range (17 - 35)
missing 14



Women: Behavioral Risk Factors
N= 2,447

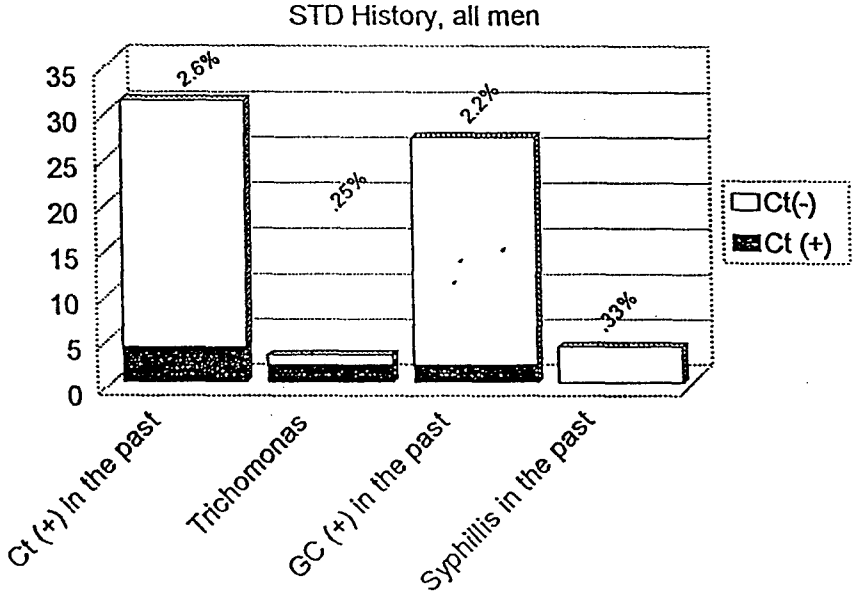
Behavioral Risk Factors	No. Of Women (%)		LCR Positive	(p-value)
Vaginal Intercourse				
yes	2273	(92.9)	9.94%	.003
no	173	(7.0)	.58%	-----
missing	1	(.04)	0.0%	-----
Symptomatic				
yes	516	(21.1)	12.2%	.011
no	1924	(78.6)	8.5%	-----
missing	7	(.29)	0.0%	-----
More than 1 sex partner, last 90 days				
yes	639	(26.1)	13.3%	.000
no	1791	(73.2)	7.9%	-----
Unknown/missing	17	(.69)	0.0%	-----
New sex partner, last 90 days				
Yes	690	(28.2)	12.2%	.003
no	1729	(70.7)	8.2%	-----
Unknown/missing	28	(1.1)	3.6%	-----
Consistent condom use, last 90 days				
Yes	365	(14.9)	8.2%	.337
no	1991	(81.4)	9.7%	-----
Unknown/missing	91	(3.7)	4.4%	-----



2,104 (86%) women did not have a previous STD. 187 (8.9%) of these women were Ct (+).

Men: Behavioral Risk Factors
N= 1,203

Behavioral Risk Factors	No. Of Men (%)	LCR Positive (p-value)
Vaginal Intercourse		
Yes	1039 (86.4)	5.7% .99
No	162 (13.5)	0.0% -----
Missing	2 (.17)	0.0% -----
Symptomatic		
Yes	41 (3.4)	19.5% .000
no	1156 (96.1)	4.4% -----
Missing	6 (.50)	0.0% -----
More than 1 sex partner, last 90 days		
Yes	406 (33.8)	8.9% .000
no	767 (63.8)	3.0% -----
Unknown/missing	30 (2.5)	0.0% -----
New sex partner, last 90 days		
Yes	441 (36.7)	7.9% .001
no	735 (61.1)	3.3% -----
Unknown/missing	27 (2.2)	0.0% -----
Consistent condom use, last 90 days		
Yes	255 (21.2)	3.1% .108
no	860 (71.5)	5.7% -----
Unknown/missing	88 (7.3)	2.3% -----



1,144 (95.1%) men did not have a previous STD. 54 (4.7%) of these men were Ct (+).

Rene Howell
12/4/97

Army Data

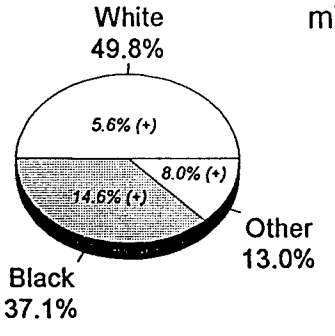
(1/21/96 through 11/23/97)
N=14,452
96.64% from Ft. Jackson (n = 13,972) 3.32% from Ft. Bragg (n = 480 enlisted)
99.99% enlisted

C. trachomatis prevalence = 9.3% (1,338/14,437)
(15 missing LCR results)

Ft. Jackson = 9.32% (1,302/13,967) Ft. Bragg = 7.52% (35/465)
PES = 9.22% (1,220/13,230) COSCOM = 7.62% (24/315)
TMC = 11.08% (82/740) Other = 7.3% (11/150)

Demographics, all women:

Mean age = 21 ± 3.80
range (17 - 46)
missing 21

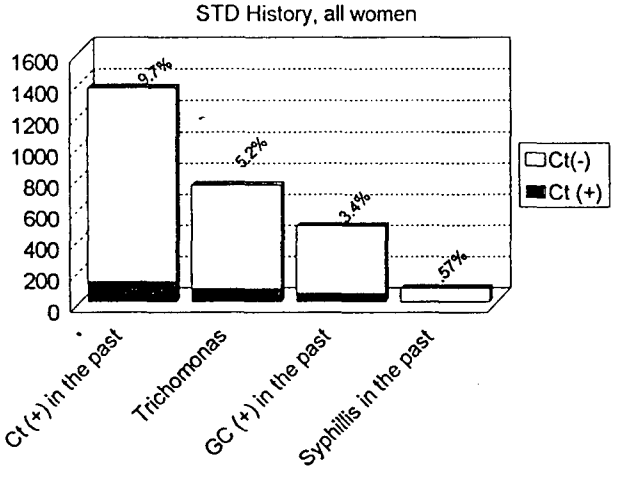


Behavioral Risk Factors, all women:

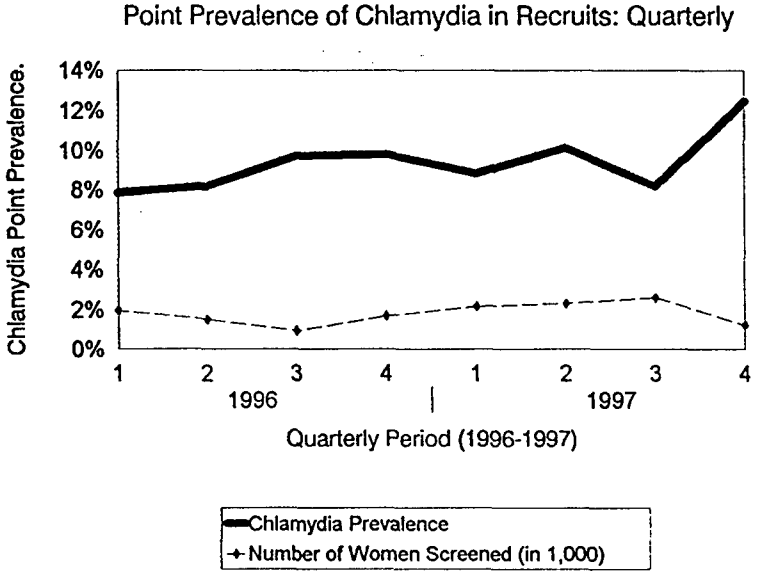
	No. Of Women (%)		LCR Positive, %
Vaginal Intercourse			
yes	13,429	(93.35)	9.81%
no	952	(6.59)	1.47%
missing	9	(.06)	11.11%
More than 1 sex partner, last 90 days			
yes	3,735	(25.84)	13.36%
no	10,541	(72.94)	7.87%
unknow/missing	176	(.568)	5.11%
New sex partner, last 90 days			
yes	4,323	(29.91)	12.35%
no	9,888	(68.41)	7.99%
unknown/missing	241	(1.67)	5.81%
Consistent condom use, last 90 days			
yes	2,383	(16.49)	8.69%
no	11,347	(78.52)	9.74%
unknown/missing	722	(5.0)	3.6%

Non-recruit
n = 1,222

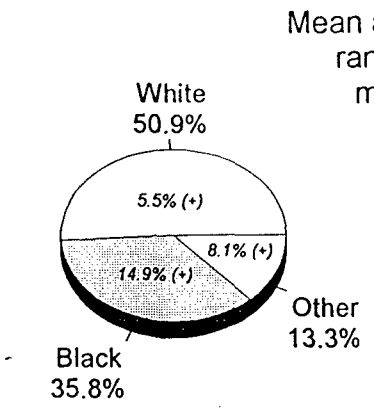
Reason for Test	Number of Women, (%)	LCR Positive, %
Contact for STD	5 (.41)	.4%
Symptomatic	4 (.33)	25%
Screening	1,206 (98.7)	9.54%
Other	3 (.25)	0%
missing	4 (.33)	



12,293 (85.06%) women did not have a previous STD. 1,115 (9.07%) of these women were Ct (+).

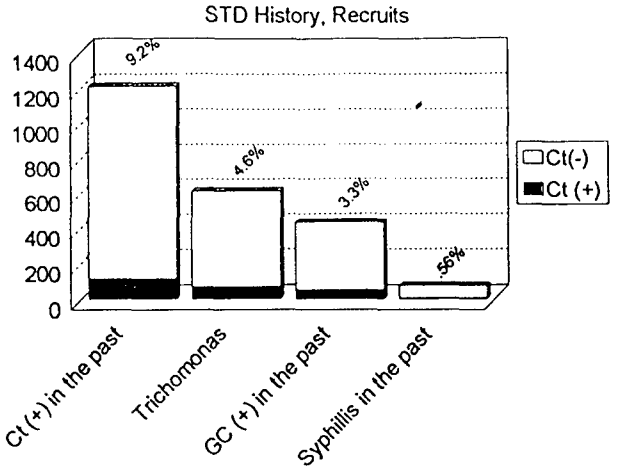


Fort Jackson, PES ONLY



Behavioral Risk Factors, all women:

	No. Of Women (%)		LCR Positive, %
Vaginal Intercourse			
yes	12,307	(93.02)	9.80%
no	914	(6.91)	1.42%
missing	9	(.07)	11.11%
More than 1 sex partner, last 90 days			
yes	3,490	(26.38)	13.50%
no	9,572	(72.35)	7.74%
unknow/missing	176	(1.27)	4.76%
New sex partner, last 90 days			
yes	4,086	(30.88)	12.38%
no	8,919	(67.41)	7.86%
unknown/missing	225	(1.70)	5.78%
Consistent condom use, last 90 days			
yes	2,118	(16.01)	8.36%
no	10,428	(78.82)	9.76%
unknown/missing	684	(5.17)	3.65%



11,392 (86.11%) women did not have a previous STD. 1,028 (9.01%) of these women were Ct (+).

Rene Howell
7/4/97

Army Data

(1/21/96 through 6/30/97)
N=10,361
95.37% from Ft. Jackson 4.63% from Ft. Bragg
(98.83% enlisted)

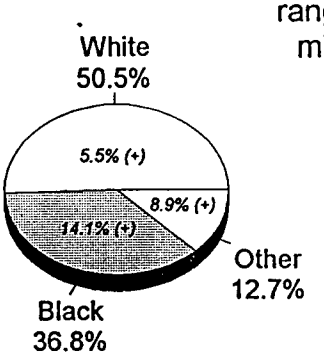
C. trachomatis prevalence = 9.10% (942/10,346)
(15 missing LCR results)

Ft. Jackson = 9.19%
PES = 8.99% (828/9,209)
TMC = 11.9% (80/672)

Ft. Bragg = 7.31%
COSCOM = 7.62% (24/315)
Other = 6.67% (10/150)

Demographics, all women:

Mean age = 22 ± 3.88
range (17 - 47)
missing 26

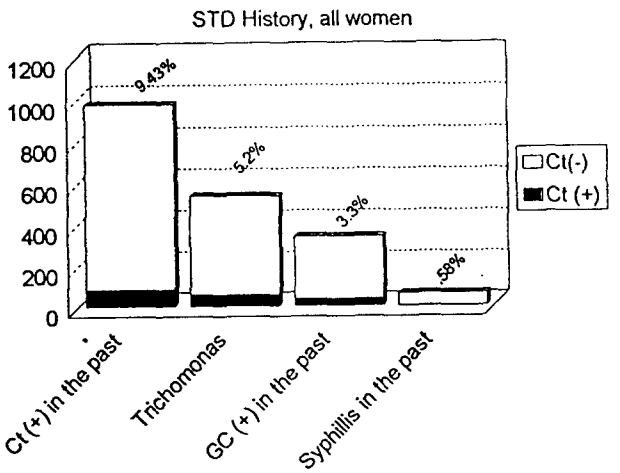


Behavioral Risk Factors, all women:

	No. Of Women (%)		LCR Positive, %
Vaginal Intercourse			
yes	9,721	(93.96)	9.56%
no	618	(5.97)	1.94%
missing	7	(.07)	14.29%
More than 1 sex partner, last 90 days			
yes	2,620	(25.32)	13.4%
no	7,568	(73.15)	7.70%
unknow/missing	158	(1.53)	5.1%
New sex partner, last 90 days			
yes	3,025	(29.24)	12.73%
no	7,119	(68.81)	7.68%
unknown/missing	202	(1.95)	5.0%
Consistent condom use, last 90 days			
yes	1,671	(16.15)	9.04%
no	8,167	(78.94)	9.43%
unknown/missing	508	(4.91)	4.13%

Non-recruit
n = 1,137

Reason for Test	Number of Women, (%)	LCR Positive, %
Contact for STD	4 (.35)	0%
Symptomatic	2 (.18)	50%
Screening	1,125 (98.9)	9.87%
Other	3 (.26)	0%
missing	3 (.26)	



8,800 (85.06%) women did not have a previous STD. 793(9.01%) of these women were Ct (+).

Rene Howell
4/7/97

Army Data

(1/21/96 through 3/31/97)
N=8,278
94.55% from Ft. Jackson 5.45% from Ft. Bragg
(98.56% enlisted)

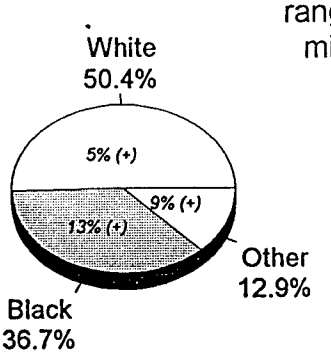
C. trachomatis prevalence = 8.76% (725/8262)
(16 missing LCR results)

Ft. Jackson = 8.84%
PES = 8.56% (616/7,198)
TMC = 12.12% (75/619)

Ft. Bragg = 7.64%
COSCOM = 7.62% (24/315)
Other = 7.69% (10/130)

Demographics, all women:

Mean age = 22 ± 4.00
range (15 - 47)
missing 20

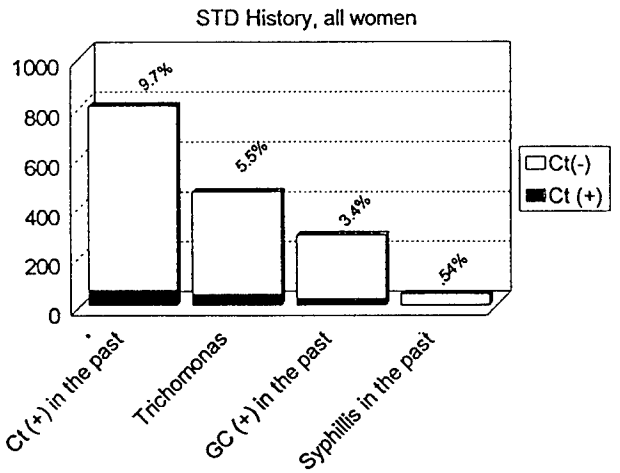


Behavioral Risk Factors, all women:

	No. Of Women (%)		LCR Positive, %
Vaginal Intercourse			
yes	7,793	(94.32)	9.15%
no	462	(5.59)	1.52%
missing	7	(.08)	.14%
More than 1 sex partner, last 90 days			
yes	2,054	(24.86)	12.37%
no	6,058	(73.32)	7.68%
unknow/missing	150	(1.82)	4.0%
New sex partner, last 90 days			
yes	2,345	(28.38)	12.03%
no	5,728	(69.33)	7.61%
unknown/missing	189	(2.29)	3.7%
Consistent condom use, last 90 days			
yes	1,305	(15.8)	9.12%
no	6,543	(79.19)	9.02%
unknown/missing	414	(5.0)	3.86%

Non-recruit
n = 1,064

Reason for Test	Number of Women, (%)	LCR Positive, %
Contact for STD	4 (.376)	0%
Symptomatic	1 (.09)	100%
Screening	1,051 (98.8)	10.1%
Other	3 (.376)	0%
missing	5 (.25)	



6969 (84.35%) women did not have a previous STD. 609(8.74%) of these women were Ct (+).

Rene Howell
11/6/97

Army Data

(1/21/96 through 10/10/96)
N=5,096
94.72% from Ft. Jackson 5.28% from Ft. Bragg
(99.61% enlisted)

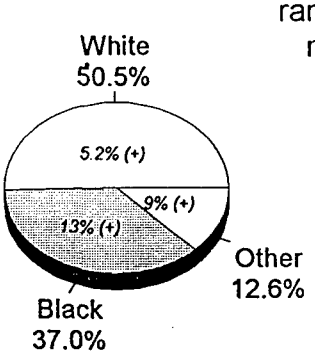
C. trachomatis prevalence = 8.56% (436/5096)

Ft. Jackson = 8.64%
PES = 8.22% (353/4296)
TMC = 12.08% (64/530)

Ft. Bragg = 7.06%
COSCOM = 7.0% (18/257)
TMC = 8.33% (1/12)

Demographics, all women:

Mean age = 22 ± 3.99
range (15 - 47)
missing 4

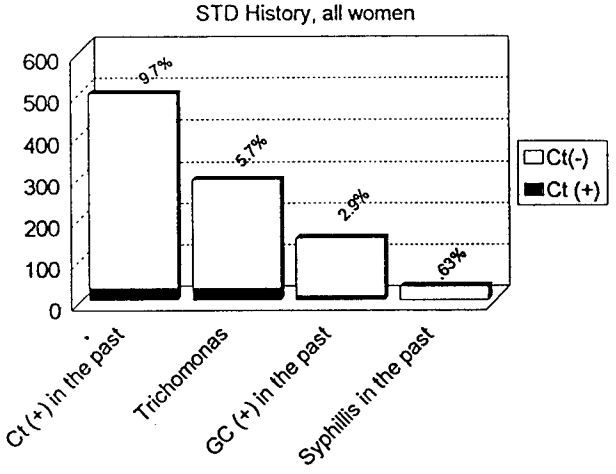


Behavioral Risk Factors, all women:

	No. Of Women (%)		LCR Positive, %
Vaginal Intercourse			
yes	4784	(93.88)	9%
no	307	(6.02)	2.6%
missing	5	(.10)	0%
More than 1 sex partner, last 90 days			
yes	1216	(23.86)	12%
no	3777	(74.12)	7.6%
unknow/missing	103	(2.02)	2.9%
New sex partner, last 90 days			
yes	1340	(26.3)	11%
no	3618	(71.0)	7.9%
unknown/missing	308	(2.71)	2.9%
Consistent condom use, last 90 days			
yes	869	(17.05)	9.2%
no	3953	(77.57)	8.7%
unknown/missing	274	(5.38)	3.3%

Women who visit either the: TMC or COSCOM
n = 799

Reason for Test	Number of Women, (%)	LCR Positive, %
Contact for STD	4 (.5)	0%
Symptomatic	1 (.13)	100%
Screening	789 (98.7)	10.3%
Other	3 (.78)	0%
missing	2 (.25)	



4284 (84.07%) women did not have a previous STD. 375(8.75%) of these women were Ct (+).

Army Data

(1/21/96 through 6/30/96)

N=3465
95.5% from Ft. Jackson
4.5% from Ft. Bragg
(98.44% enlisted)

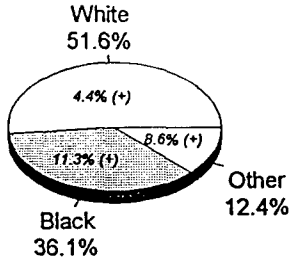
C. trachomatis prevalence = 7.42% (257/3465)

Ft. Jackson = 7.49%
PES = 7.3% (232/3187)
TMC= 13.2% (16/121)

Ft. Bragg = 5.8%
COSCOM = 5.8% (9/156)

Demographics, all women:

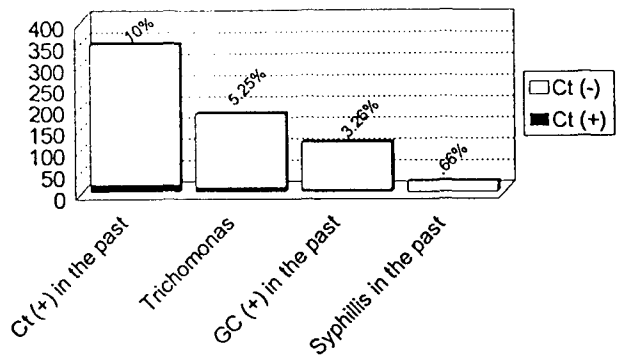
Mean age = 22 ± 3.89
range (17 - 47)



Behavioral Risk Factors, all women:

	No. Of Women (%)		PCR Positive, %
More than 1 sex partner, last 90 days			
yes	792	(22.86)	9.6%
no	2597	(74.95)	6.9%
unknow/blank	76	(2.19)	4.0%
New sex partner, last 90 days			
yes	858	(24.76)	9.4%
no	2505	(72.29)	6.9%
unknown/blank	102	(2.94)	2.9%
Consistent condom use, last 90 days			
yes	597	(17.23)	8.7%
no	2683	(77.43)	7.27%
unknown/blank	185	(5.34)	5.4%

STD History, all women



2908 (83.92%) women did not have a previous STD. 226 (7.77%) of these women were Ct (+).

Preliminary Report

Army Data:
1/21/96 through 3/3/96

N=1265

Overall *Chlamydia trachomatis* prevalence: 6.9%

Jackson: 6.88%
PES: 6.6%
TMC: 13.04%

Bragg: 6.89%

95.3% from Ft. Jackson
4.6% from Ft. Bragg

99.4% enlisted

47.4% White
39.2% Black
13.4% Other

94% have had vaginal intercourse

23% have had more than 1 sex partner over the past 90 days
74.8% have not
2.2% did not answer

22.1% have had a new sex partner over the past 90 days
74.8% have not
3.0% did not answer

78.4% have used condoms during every sex act over the past 90 days
16.9% have not
4.6% did not answer

10.7% have had ever been diagnosed with Chlamydia
3.3% have ever been diagnosed with Gonorrhea
.47% have ever been diagnosed with syphilis
5.7% have ever been diagnosed with Trich
82.5% have never been diagnosed with any of these STDs

11.6 Scantron Instrument

CHLAMYDIA PROJECT

Chlamydia Laboratory – Ross 1164 Johns Hopkins University
Division of Infectious Disease • School of Medicine
720 Rutland Avenue • Baltimore, MD 21205-2196

USE NO. 2 PENCIL ONLY

SOCIAL SECURITY NUMBER — or ○ Anonymous

RANK
- ○ Enlisted
  - ○ E1-3
  - ○ E4-6
  - ○ E7-9
- ○ Officer
  - ○ 01-03
  - ○ 04-07

DATE OF BIRTH

Month	Day	Year

RACE
- ○ White
- ○ Black
- ○ Amer. Indian or Alaskan
- ○ Asian/Pacific
- ○ Other

HISPANIC?
- ○ Yes
- ○ No
- ○ Unknown

STUDY TYPE
- ○ Prev
- ○ Select
- ○ Universal

CATEGORY
- ○ RA
- ○ NG
- ○ AR

POST PROJ AREA
- ○ Jackson
- ○ Bragg

CLINIC-SITE ID

VISIT TYPE
- ○ FP
- ○ STD
- ○ Basic in Process
- ○ Annual Gyn Visit

SEX
- ○ Male
- ○ Female

LAST NAME

FIRST NAME

MI

ADDRESS (UNIT)

CURRENT ZIP CODE

PREVIOUS STATE

PREVIOUS ZIP CODE

SURVEY CONTINUED ON SIDE 2 . . .

Ever Had Vaginal Intercourse?
- ○ Yes
- ○ No

Within the Past 90 Days

More Than 1 Partner	New Sex Partner	Condom Use With Every Sex Act
○ Yes	○ Yes	○ Yes
○ No	○ No	○ No
○ Unknown	○ Unknown	○ Unknown

Ever Been Diagnosed With
(Mark all that apply)
- ○ Chlamydia
- ○ Gonorrhea
- ○ Syphilis
- ○ Trichomonas
- ○ None

Symptoms: ○ Yes ○ No

Reason for Test
(Mark All That Apply)
- ○ Known Contact to STD
- ○ Suspected Contact to STD
- ○ Any Symptom of STD
- ○ Screening
- ○ Rescreening
- ○ Other

DATE OF SPECIMEN COLLECTION

Month	Day	Year
01	01	○ 96
02	02	○ 97
03	03	○ 98
04	04	○ 99
05	05	○ 00
06	06	
07	07	
08	08	
09	09	

Source of Specimen(s)
- ○ Cervix
- ○ Urethra
- ○ Rectum
- ○ Urine
- ○ Vaginal
- ○ Other

Clinical Presentation
(Mark All That Apply)
- ○ Mucopus
- ○ Cervicitis
- ○ Ectopy
- ○ Cervical Motion Tenderness
- ○ Friability
- ○ Pregnant
- ○ Normal Exam
- ○ No Exam

Was Patient Presumptively Treated for CT Based on Clinical Findings?
○ Yes ○ No

Was Patient in Mass Therapy Group?
○ Yes ○ No

TEST RESULTS

STUDY ID NO.

LAB ID NO.

DNA Amplification
- ○ Negative
- ○ Positive

Culture Other
- ○ Negative
- ○ Positive
- ○ Toxic

DNA Probe
- ○ Negative
- ○ Positive

DFA
- ○ Negative
- ○ Presumptive Positive
- ○ Positive

EIA
- ○ Negative
- ○ Presumptive Positive
- ○ Positive

Condition if Unable to Process
- ○ Broken/Leaked in Transit
- ○ Inadequate ID/Slip Detail
- ○ Inappropriate Specimen
- ○ Not Viable
- ○ Inadequate Specimen

Person Performing Test:_____

Date of Test:_____

11.7 SAS Questionnaire

(FOR NURSE) Study No:_____

CHLAMYDIA PROJECT

Chlamydia Laboratory -Ross 1164 Johns Hopkins University
Division of Infectious Disease-School of Medicine
720 Rutland Avenue-Baltimore, MD 21205-2196

Lastname: _____ Firstname:_____
Date of birth:_____

Collection Options:

The following questions refer to your preferences regarding collection of urine and self-administered vaginal swabs---

1. Which of the two collection methods (urine or self-administered vaginal swab) did you think was the easiest to use?
   (circle one) urine self-administered swab
   Why? _____

   _____

2. Did you feel comfortable doing the following method?

urine (circle one) yes no

self-administered swab (circle one) yes no

On a scale from 1 to 10 (1 is not uncomfortable and 10 is very uncomfortable) how would you say you felt collecting each?

urine:

1 2 3 4 5 6 7 8 9 10

not uncomfortable ←----------→ very uncomfortable

self-administered swab:

1 2 3 4 5 6 7 8 9 10

not uncomfortable ←----------→ very uncomfortable

CONTINUE ON OTHER SIDE

3. Would you collect the following **at home** if you thought you might be infected with chlamydia?

urine	(circle one)	yes	no
self-administered swab	(circle one)	yes	no

4. Would you collect the following **in the field** if you thought you might be infected with chlamydia?

urine	(circle one)	yes	no
self-administered swab	(circle one)	yes	no

5. Did you have any objections to using the urine method:

- uncomfortable catching the urine in the cup
- uncomfortable carrying the urine in the cup
- painful
- other: _____

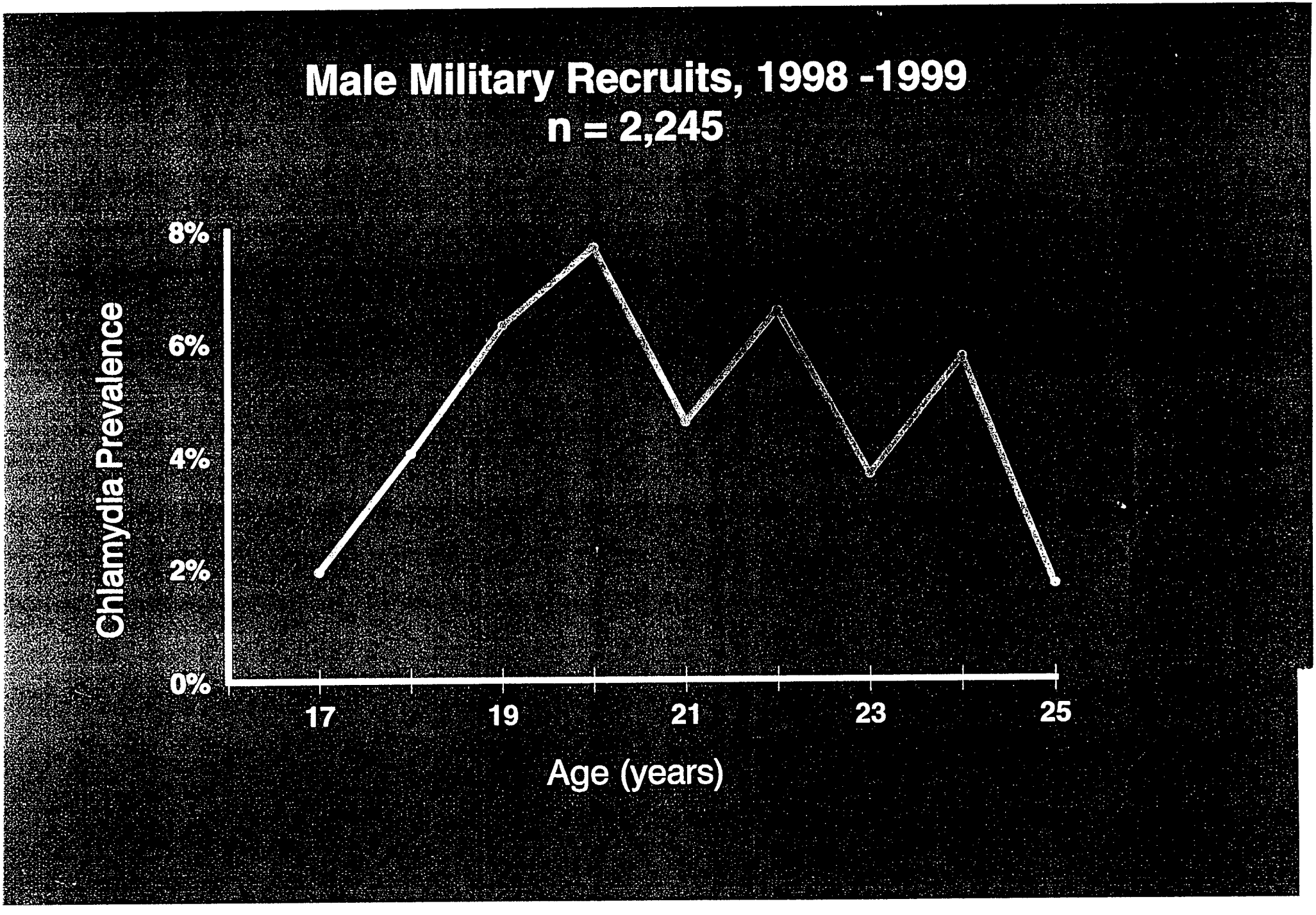
6. Did you have any objections to using the self-administered swab method:

- uncomfortable doing the self-administered swab
- uncomfortable carrying self-administered swab
- painful
- other: _____

7. In the following three locations if you had to choose one method which would you prefer to use:

Location:	(circle one for each place)		
1) **clinic**	urine	*or*	self-administered swab
2) **home**	urine	*or*	self-administered swab
3) **field**	urine	*or*	self-administered swab

11.8 Male Prevalence by Age, 1996-1999


Male Military Recruits, 1998 -1999
n = 2,245
Chlamydia Prevalence
8%
6%
4%
2%
0%
17
19
21
23
25
Age (years)

12 Final Report

Bibliography Of Publications (see appendices and section 8 "Reportable Outcomes)

Bibliography Of Presentations And Abstracts (see appendices and section 8 "Reportable Outcomes)

List Of Personnel Receiving Pay From The Research Effort:

1. Charlotte Gaydos, Principal Investigator
2. Anne Rompalo, Co-Investigator
3. Dorothy Ellis, Health Research Nurse
4. Pamela Syffus, Health Educator
5. Eleanor Howard, Research Nurse
6. Katherine Cline, Research Nurse
7. Bobbie Lynn Jones, Research Nurse
8. Martha Alsup, Research Nurse
9. Sandra Leister, Laboratory Technician
10. Diana Perkins, Laboratory Technician
11. Dien Pham, Laboratory Technician
12. Graciela Jaschek, Laboratory Technician
13. Jennifer Tawes, Laboratory Technician
14. Melissa Theodore, Laboratory Technician
15. Rene Howell, Data Analyst/Cost-Effectiveness
16. Samantha Johnson, Data Entry
17. Jowyna Daniel, Data Entry
18. Barbara Pare, Study Coordinator
19. Kimberly Riely, Research Assistant
20. Shakara West, Research Assistant